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TABLE OF CONTENTS

Our Concern For The Mind LORD ADRIAN, O.M., M.D., F.R.S. 78

Assessment of Respiratory Failure in Poliomyelitis R. V. WALLEY, M.D. 82

Excretion of Electrolytes During Intermittent Positive-Pressure Respiration JOHN MARSHALL, M.D., F.R.C.P.Ed., M.R.C.P. 85

Tuberculosis Control in Denmark H. FRANKS, M.B., D.P.H. 87

Hazard in Use of Beaver Ventilator E. H. FRANKS 91

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BRITISH MEDICAL JOURNAL

LONDON SATURDAY JULY 25 1959

OUR CONCERN FOR THE MIND

BY

LORD ADRIAN, O.M., M.D., F.R.C.P., F.R.S.

Master of Trinity College, Cambridge, and Vice-Chancellor of the University of Cambridge

It would be wrong not to begin by thanking you for inviting me to give this address. I am as proud as everyone here to belong to our worthy profession, and, as I have lived an academic life in the rear of the front line, I am doubly proud to be chosen by those who are in the thick of it. It is an honour which no one should have accepted out of hand, for it involves an obligation not merely to speak but to have something to say. So I had better confess that I wasted no time over such scruples: the prospect of this meeting was so pleasant that I had not the will to refuse.

There are many things that make it pleasant for all of us — the drive through the Border country, the romantic capital we have come to, and the friends we meet in it, but my own particular reason for pleasure is more compelling. It is that I attended my first scientific congress here in 1923 with my wife, and that we were newly married and going to set up house as soon as we were back in Cambridge. I will say no more about that domestic angle, for even without it there would be vivid memories to recall. The world was coming back to life after the first world war and we were joining the International Congress of Physiology. Congresses were still small enough to be family parties, and we were received into the party by Schafer and his Edinburgh colleagues with all the well-known physiologists as fellow guests. Pavlov had come to talk about conditioned reflexes, with his son as interpreter; Magnus demonstrated the righting reactions of the guinea-pig. Biochemistry was still part of the family, and diabetes was as good as conquered by Banting and Best. In fact, physiology was booming: the meeting was a grand start for a young couple, and I feel sure that the sun shone uninterruptedly.

That was thirty-six years ago, and now instead of congresses of about 300 there is the Physiological Congress of over 2,000; the pharmacologists have their own; the biochemists run to 5,000 or more; and there are so many smaller meetings for the specialists that it is a wonder that they have any time in their laboratories. And, in spite of that, an immense volume of research has gone on in every branch of medical science and there have been spectacular advances in the treatment of disease. Advance would certainly have come if the world had been able to live at peace, but it is remarkable how much of the advance seems to have been the direct result of two great wars.

War and Medical Progress

If our descendants are able to live at peace with one another they may not realize the full effect that war can have on medical progress. They will realize why there were technological advances in everything connected with fighting and why the medical services had to be specially concerned with the diseases of armies in unhealthy conditions as well as with the injuries they inflict on one another. They will see why it was necessary to eradicate malaria, with the resulting increase of the areas which can be inhabited by man; for this, after all, has been the result of earlier wars on a more limited scale: without the Spanish-American War at the turn of the century we should have had to wait much longer for the attack on yellow-fever and hookworm, and we can confidently expect that more uninhabitable regions will be made habitable if there are further wars of the sort that will find a use for them.

But we all know that this is nothing like the whole story. Our descendants will realize some of the emotional strains engendered by wars in those who had to risk their lives or self-respect, but even for us it is hard to recall the full force of the emotional drive which diverted the world from contemplation to action.

In 1914 and 1939 scientists in every field lost interest in the distant target and moved heaven and earth for a chance to put their skill to some practical use. Their particular loyalties assured them that the only way to true progress was to strike down the enemy.

What was achieved under this emotional pressure has altered the whole pattern of scientific advance. In physics and chemistry as well as in medicine the two great wars encouraged practical applications, and their solution has reacted on theory. And although some lines of academic research may have suffered, I think we should all agree that the infusion of new ideas has been to the general advantage.

No one wants the world to be in a constant state of emergency where only the most detached scientist could keep his interest fixed on the stars. The diversion to short-range problems could not have succeeded without the peace-time knowledge to glean from, and in peace-time many scientists work in fields where no one will be much the worse if the practical applications are neglected. An intensive development of them might lead to faster travel or shinier fabrics, but we can afford to wait for these benefits until the advertisements force them on our notice.

In the medical field we cannot be quite so complacent, for the sick are always there to claim the immediate application of new knowledge; but in medicine

[*] Address given at the Adjourned Annual General Meeting of the British Medical Association at Edinburgh on July 20

there is another way in which the pressure of war has helped the advance: it has done so by focusing attention on old problems as well as by diverting it to new ones. We have many old problems which we are liable to neglect because they are old and have been difficult to solve in the past, or because they arose from social conditions which were taken for granted. For there is a special brake on medical progress which has encouraged us to let them alone—the brake which is imposed by the ingrained resignation of the human race in the face of ill-health.

We still need resignation to face the disabilities of our old age and its final termination, and early views of disease have very deep roots in the mind. Though we have learnt to relate our ailments to natural and not supernatural influences, there is still the image of Nature as a stern goddess upholding the way of life our forefathers were used to. In Edinburgh one does not need to be reminded of the critics of Simpson who thought it wrong to do away with the pains of childbirth. And we do not need to consult statistical tables to recall the infantile mortality that we tolerated at the beginning of this century.

The war of 1914 showed how Nature had dealt with the population of the British Isles. It compelled a stocktaking of the health and physique of our adult males, and it was a shock to the public as well as to the medical profession to realize the great number who had to be classed as C3 instead of A1. Since they had been C3 from childhood it was then too late to find a remedy. The lesson, fortunately, was not forgotten in the 20 years of peace, though the second war was needed to establish proper dietary standards.

Mental Health

There was another neglected field of medicine to which the first war drew our attention, for it became necessary to consider the mental as well as the bodily health of our armies. When the war was over the emotional origin of many symptoms was recognized, and their recognition no longer meant that they were to be dealt with by a tonic or a refusal to take them seriously. I am afraid there can be no certainty that our mental health has been greatly improved, but I think it will be worth spending time to discuss the change in our attitude to it. It is a chapter of medical history which shows what the pressure of war can do and how it must be followed by the slower building up of knowledge in more peaceful times.

By 1914 Freud's work was already well advanced. English translations were available and Ernest Jones had begun to shock conventional opinion by insisting that they should be taken seriously. Bernard Hart had prepared the way in 1912 by publishing a small classic, *The Psychology of Insanity*. It was widely read by laymen as well as doctors and seemed to put psychiatry on a new footing. On the Continent it had already become an important field for research and here no doubt the new ideas would have taken hold sooner or later, but until the war the neuroses attracted very little interest. Patients who could afford them were allowed to do so. Neurologists were satisfied if they could exclude organic disease of the nervous system, alienists signed certificates, and there were a few enthusiasts, well regarded but without hospital posts, to whom cases were referred for treatment. There was the Weir Mitchell rest cure for neurasthenia, there were some reputable hypnotists and many medicinal spas.

Emotional Origin of Shell Shock

The war changed all that within a few months when shell shock became an urgent military problem. It was supposed at first to be due to mechanical damage to the brain and treated by prolonged rest, but the realization of its emotional origin did not make its treatment and prevention less urgent. Within a year most of the convalescent hospitals on this side of the Channel had spectacular cases to display of mutism, deafness, tremors, paraplegia, convulsive attacks — the whole gamut of hysterical manifestations elaborated by Charcot at the Salpetrière. Our French colleagues had the same war-time experience, and displayed their usual skill in devising categories with appropriate names: camptocormie, dysbasie, tremblements, pseudo-choreiformes, etc.

For those who were new to these dramatic symptoms it was at first an immense attraction to work the miracle which restored the patient to bodily health. There was great variation in technique, ranging from persuasion or hypnosis to some face-saving suggestive method; but a feature of the most successful kinds of treatment was the unrelenting pressure which was maintained until every physical symptom was abandoned. The brain-washing technique which produces the full confession and change of heart has been compared by Sargant to some revivalist procedures, and one can see a considerable resemblance in some of the methods which were used to dispel the amnesias and palsies of the first war. They are well described in Arthur Hurst's writings in 1918 and in Roussy and Lhermitte's in 1917.

But unfortunately hidden fears were seldom banished by blocking this path of escape. Special hospitals had to be set up, close to the front line, to prevent the elaboration of hysterical symptoms, and they were staffed by doctors specially interested in the psychological side of medicine and in the way in which these symptoms arose.

The Freudian Outlook

During the war Freud's theories remained in the background. They could not be overlooked, since they suggested a possible line of treatment, and they were brought into some prominence by the savage contempt of the orthodox. But it was not a congenial time for pursuing the sexual symbols appearing in dreams or for arguing that an unconscious mind was a contradiction in terms. The lengthy processes of psycho-analysis were out of the question, but those who had not taken sides and were prepared to experiment found enough to rouse their interest in the Freudian outlook or at least in the mental processes which Freud had described. The recall of distressing experiences seemed to be a useful, perhaps an essential, step for the reassurance of the patient, and it was only too obvious that the hysterical escape from anxiety was more intelligible in psychological than in physical terms. By the end of the war the methods adopted in most of the special hospitals did not differ much from those in use in the last war, though in those days the range of sedatives and of physical methods of treatment was far more restricted.

The change in our attitude to neurosis came gradually and might have been longer in coming without a paper in The *Lancet* in 1917 in which Rivers stated the psychological position with admirable restraint — and restraint was needed, for the enthusiasts were already gathering to overplay their hand.

They did so with increasing vehemence after the war, and issues were further confused by the diverging gospels of Jung and Adler, and for a brief space by the popularity of Coué, a simple and honest faith healer. By that time, however, the tide was running strongly in favour of the emotional origin and elaboration of neurotic illness on the lines described by Freud. It is still running strongly, and it would need great self-assurance now to deny any value to his interpretation. Most of us have had to take its details on trust, for the literature is extensive and often obscure, and until we have mastered it and perhaps been analysed ourselves we are in no position to criticize the psycho-analysts. Their practice demands a long training and long sessions with their patients. It is not their fault that they must lead dedicated lives which give no time for scientific propaganda. But we can agree that we have all gained a new way of regarding human behaviour from the cradle onwards, a new aspect showing all kinds of detail as part of a coherent picture. The picture may be distorted and there are other aspects to be considered, but that does not alter the fact that it has made us revise all our notions of parental and social responsibilities and given us new kinds of biography and interpretations of historical events.

The first war provided a large-scale demonstration of psychical and psychosomatic illness and of the effects of different kinds of treatment. But the history of medicine makes us look very carefully before we should agree that the particular line of treatment has much to do with its results. In the past, success in the treatment of neurotic complaints had been claimed for methods as different as the removal of the colon, the anchoring of a wandering kidney, and the laying on of hands. Without statistics, and with the fortunes of war changing from month to month, the evidence in favour of treatment by abreaction was not convincing proof of the theory behind it, and, as Rivers pointed out in 1917, the investigation of war neuroses had really done very little to support the overwhelming importance of the sexual theme.

In fact, I think our attitude to neuroses changed as the war went on, not so much because of what we found in our patients but because of what we were finding in ourselves. It was a time for the recasting of ideas. We had lost faith in the rule of our elders and were fighting a war which seemed to have no meaning and no end. The Freudian picture fitted the mood of disillusion. It meant a radical change of outlook away from the concrete but unenlightening details of physiology and pathology to an allegorical representation of the mind with veiled and rather sinister figures contending for mastery. We could imagine these forces at work in ourselves, and Freud had given them substance by showing how their conflict could explain neurotic as well as normal behaviour. To be sure, the great French neurologists had interested themselves in hysteria, but it led no further to say that it came from increased suggestibility. The Freudian scheme, with its unflattering picture of human motives, was a challenge bound to be taken up, and it was a new and comprehensive explanation with enough detail to be examined dispassionately.

New Lines of Attack

It is not surprising, therefore, that the first war made us turn to the repressed complex as a cause of ill-health, but it is also not surprising that thirty years of peace interrupted by another war have given an opportunity for exploring other lines of attack.

They began as the result of clinical observations unrelated to any theory, for Sakel found the effects of insulin coma almost by accident, and Meduna tried camphor-induced convulsions because an epileptic fit seemed to benefit schizophrenia. In 1933 the reports of these new treatments of mental disease seemed a reversion to the eighteenth century. There was nothing but the results to justify them: yet in this case the proof of the pudding has been the eating, and electrically induced convulsions have become the routine method for freeing the mind from some of its troubles. Here the point of attack is the brain and not the conflict of ideas which has arisen in it, and leucotomy and the tranquillizing drugs are in the same category: it is their action on the brain which relieves the over-anxious mind.

If we agree, as we must, that brain and mind interact or run in parallel, it is rational enough to aim at reducing the conflict by psychotherapy or by damping down the neural activity without which it cannot exist. But at present we still have these two sides of the picture to choose from. We tend to blame the mind when the disturbance is slight and the brain when it is more severe, though we show our confusion by calling the slight disturbance a neurosis and the severe one a psychosis. And our former wars have been responsible for emphasizing the present dilemma. It is owing to them that the picture drawn by Pavlov has taken so long to become fashionable in the West and that the picture drawn by Freud has scarcely begun to penetrate to the East.

Pavlov's Physiological Picture

Pavlov's interpretation of human behaviour has been accepted in the East far more whole-heartedly than Freud's in the West. It has inspired an immense volume of research and a large Russian literature. It is the basis of the treatment used for all kinds of mental disturbance and for all the problems of childhood and adolescence. Pavlov was an unrivalled experimenter, a skilled surgeon with abounding spirits and good health, and he took a more cheerful view of our troubles than Freud. Our anxieties are not considered as the symbolic expression of what we must not allow ourselves to think; for the mind, conscious or unconscious, has no place in his scheme. Our intelligent behaviour expresses our cerebral activity, and our troubles are due to some derangement of the processes of conditioning and of the balance of excitation and inhibition of the cerebrum. On both schemes we can blame our special troubles on the way we have been brought up, but in the East the emphasis is on the nervous connexions and not on the original sin.

Unless we are as whole-hearted materialists as our colleagues in the East we must think of Pavlov's scheme as a working hypothesis for analysing behaviour from the physiological side. The picture before us is that of a nervous machine which can make intelligent decisions. The picture does not go into details, but the outlines are based on evidence which can be tested experimentally, and to that extent it has the advantage over the psycho-analytic picture of the mind. This may offer an explanation of every detail in a dream, but the evidence is seldom of a kind to give complete certainty, and it is difficult to see how the picture can be devel-

oped much further. The physiological picture is still in the making, and we have a long way to go before the advance from this side will be halted.

What Does the Brain Do?

The difficulty at present is that the advance is leading us into a wood that becomes more and more obscure because the trees are so thickly crowded. Work in the physiology and biochemistry and pharmacology of the brain has accumulated a great store of facts, and neurosurgery can now check them on the human patient. The result has been that the simple schemes which used to satisfy us are as out of date as the maps of the phrenologists, but as yet we have nothing much better to take their place. In fact, we really have no clear idea of what most of our brain does for us, of the part it plays in guiding our thought and behaviour. Some areas receive signals from the sense organs or elaborate skilled movements, but there is a duplicate or even a triplicate representation, and in animals most of it can be destroyed without obvious loss. Large areas of the human cerebrum can be destroyed without making us incapable of rational thought or behaviour. The electroencephalogram seemed to herald a new way of analysing cerebral activity, but it has revealed little more than the tendency to epilepsy. Micro-electro recordings from the nerve cells of the cortex give a bewildering variety of response patterns. The search for chemical transmitters is still going on, and every day the psychiatrists gather in the new drugs and enzymes which might furnish information that would help them in their investigations.

This is, of course, a most enviable position to have reached. The obscurity is a challenge. It throws no gloom on the investigator, and no one doubts that there will soon be new discoveries to bring us into the light again. Just at present, however, I think we have gone too far to use Pavlov's formula without a good deal of revision, and we have certainly not gone far enough to be within sight of any blending of the two pictures —finding the nervous substratum of the id and the super-ego or localizing the censorship of thought in the reticular formation.

Our treatment seems to recognize the possibility of it, for it mixes drugs and convulsions and neurosurgery with psychotherapy and psycho-analysis; and there is nothing new in this: the bottle of medicine and the doctor's visit have made the two-pronged attack for centuries. And we have progressed in understanding far enough to have no further use for the methods of dealing with hysterical manifestations which were developed in the first war. We have made our mental hospitals much more cheerful places to visit, and though they have many more patients the majority are soon able to leave. But we do not seem to have checked the incidence of disorders for which the brain or mind is mainly responsible. We are badly in need of new discoveries in the pathology of the brain and of fresh developments on the psychological side to bring the two pictures nearer together.

We cannot now expect another major war to give a fresh turn to our thoughts: there will be no more large wars to alter the course of arts and sciences, for when they have finished there will be nothing left to alter. But there is still a long way to go on a dual but converging attack. There is no reason to doubt that the normal progress of laboratory and clinical research will give the answer for those mental disorders that have an organic origin. It has done so already for general paralysis of the insane: the biochemistry of the brain is still in its infancy, the lysergic acid story has raised our hopes and gamma amino-butyric acid is a strong candidate for the role of a humoral inhibitory agent. And on the psychological side, though research is more difficult, the paediatrician and the child psychiatrist may devise methods of upbringing with fewer perils to the mind. We must learn more about the effect of social pressures, the particular conditions in our own ways of life and in human society generally which lead to anxiety or psychosis.

Medical Aspects of Social Problems

In fact, we have still a long way to go in the path of advance which was opened up after the war of 1914 by the shell-shocked patients, the change in our attitude to neurosis, and the theories of Freud and Jung and their fellows. Elaboration of the Freudian picture may not lead much further, but this does not mean that we cannot learn better ways of ensuring mental health, better ways of dealing with the frustrations of infancy, the revolts of youth, and the loneliness of old age. Social science, and its applications to medicine, may have been poorly served by the enthusiasts, and some of their conclusions have been criticized as vehemently as we were once accustomed to criticize Freud. In spite of that, the medical profession has established its right to a hearing in a wide range of social problems which were formerly the exclusive province of Church and State. We must not set ourselves up to instruct the teachers, the criminal courts, and the law givers on matters about which we have no clear views ourselves, but at least we know more than they do about the physics and chemistry of human behaviour and about the mental tensions which can menace it.

For increasing our knowledge of these things we must rely mainly on the research teams who can make the experiments and the statistical surveys and give their whole time to investigation; but the interactions of mind and body are more likely to reveal themselves in the surgery and the consulting-room than in the laboratory. It would be a great mistake to think that there can be a general advance without the support of every doctor who has patients to understand. We have ourselves to understand too: however healthy and well balanced we may be there may be something to learn by observing our own reactions to difficult situations. At all events we have been trained to the clinical observation of human beings exposed to anxiety and discomfort, and we must not belittle our training.

Our two great wars and the years that have followed them have given us new methods and ideas and a better nourished and healthier population to look after. We need not worry too much at having found no answer to an old philosophical dilemma, but we have patients with troubles to be prevented or put right, and we have learnt to respect troubles that we used to neglect. Our medicines for them have longer names and our psychotherapy is more self-conscious, and we have still a long way to go before we can claim any striking advance. But it is our privilege as well as our responsibility to work for it, and it will be a work in which every one of us can share.

ASSESSMENT OF RESPIRATORY FAILURE IN POLIOMYELITIS

BY

R. V. WALLEY, M.D.

Ham Green Hospital, Bristol

The chief danger to life in poliomyelitis is respiratory failure. This may come about in two ways: firstly, by paralysis of the intercostal muscles and diaphragm; secondly, by obstruction of the airway as a consequence of paralysis of the muscles concerned with swallowing, which is the most important feature of involvement of the spinal bulb. The fatal cases most often have both forms of paralysis. At the onset of failure, and often throughout, the lungs are normal. This is in contrast to respiratory failure occurring in chronic bronchitis, when lung compliance and gas distribution and diffusion are affected. The successful treatment of respiratory failure in poliomyelitis calls for an accurate assessment of respiratory function. During the past five years at Ham Green Hospital we have admitted 62 cases of respiratory and bulbar paresis due to poliomyelitis. In treating these cases we have made use of standard methods of studying respiratory function in addition to clinical observation. This paper is based on our experience with these cases

Clinical Assessment

Failure of swallowing can be best diagnosed by observing the pooling of secretions in the pharynx. Inhalation of these secretions and airway obstruction will occur unless steps are taken to prevent them, and such cases may present with acute dyspnoea and with many rales to be heard in the chest, or as patients whose respiration in the tank respirator is unsatisfactory.

Clinical assessment of failing respiration, apart from airway obstruction, must be considered in terms of respiratory function and not of recognition of abnormal physical signs. The respiratory reserves are large and must be greatly reduced before the patient is distressed. The adult poliomyelitis patient at rest in bed needs only 6–8 litres of ventilation a minute. The maximum voluntary ventilation under test conditions ranges from 120 to 180 litres a minute in normal adults. The eye can only crudely estimate the extent of the thoracic movement, while the diaphragm, whose movement produces three-quarters of the vital capacity (Wade, 1954), cannot be directly observed at all. A function test is therefore required, and we employ the following one on all patients with paralytic poliomyelitis. The patient is asked to take a deep breath and count aloud at the rate of two digits a second as high as he can before taking another. A demonstration by the physician serves to standardize the test. We have found, as have others (Plum, 1952), that when an adult patient can only count up to 20 his vital capacity has fallen to about 2,000 ml., when he can only count up to 15 it has fallen to about 1,500 ml., and so on. Observation of the power of coughing is another less precise function test.

Through function tests alone can give an accurate early assessment of respiratory weakness, they cannot be used with patients under the age of 6. Our experience has shown that if these children have no definite arm weakness, if they can cry loudly, or sleep soundly, they have no need of artificial respiration.

The value of clinical observation, again, is limited in accurately determining the efficacy of artificial respiration. For various reasons we have overventilated patients for considerable periods to the extent that the arterial carbon dioxide tension fell to 20–30 mm. of mercury (normal 38–42), and they showed no abnormal signs or symptoms. On only one occasion have we seen tetany with tingling of the extremities. Underventilation will be quickly recognized by the conscious patient, though he may complain of "not getting enough air" when his arterial blood gas levels are normal. On some occasions underventilation may be suspected when the patient attempts to breathe on his own in between or against the cycles of the respirator. If the ventilation provided by the respirator is increased he may synchronize satisfactorily, his own efforts being no longer stimulated by accumulated carbon dioxide. However, the clinical signs of underventilation—that is, the signs of anoxia and hypercapnia—appear only when underventilation is gross.

Cyanosis can be detected in a good light only when the haemoglobin saturation falls to 70–80% of normal. Owing to the S-shaped dissociation curve of haemoglobin, this fall in saturation is the result of 50% fall in oxygen tension. When oxygen is administered the fall in tension may not occur, although hypercapnia, due to underventilation, may be present. A sudden rise of carbon dioxide tension, if large enough, may produce flushing, sweating, and a rise in blood pressure, but estimation of arterial carbon dioxide tension has shown us that these signs are only a rough guide to the recognition of underventilation. For example, a patient under our care developed a sudden rise of carbon dioxide tension up to 65 mm. of mercury and showed none of the above signs. In addition, flushing, sweating, and hypertension (McDowell and Plum, 1951) may be due directly to the infection

Laboratory Methods of Assessment

Spirometry.—Of the techniques used to estimate respiratory function in poliomyelitis, spirometry is the most valuable. It is used principally to measure the vital capacity and tidal air. Measurement of maximum voluntary ventilation and related figures (Gandevia and Hugh-Jones, 1957) may provide information of value in some cases. For the measurement of vital capacity we have found the Hutchinson waterbell spirometer most suitable, and use a small one with a 2.5-litre bell instead of the more usual 6-litre bell. The gas-meter spirometer is more convenient to use, but the two commercial types we have tested were inaccurate for small single volumes. We use a small-volume-recording spirometer with variable drum speed for measurement of the tidal air and very small vital capacities. The bell is exactly half the standard size, and so standard recording charts can be quickly interpreted. At the time of writing a small accurate flowmeter designed by Wright (1955) has been introduced by the British Oxygen Company which promises to be very suitable for clinical measurement of vital capacity and tidal air. For measurement of maximum voluntary ventilation we use an apparatus designed by McKerrow (1953). For peak expiratory flow, a related value, another small apparatus has been designed by Wright.

Estimation of Arterial Blood Gases.—We have been estimating arterial blood gases routinely in these cases during the past two years (Walley, 1957). The total carbon dioxide content and *p*H are measured, and from these values the carbon dioxide tension is calculated. The oxygen saturation is measured by a cuvette oximeter.

Estimation of End Tidal Carbon Dioxide Content.—Under normal lung conditions the carbon dioxide content of the air expired at the end of a normal tidal expiration is the same as that in the alveolar air, which is in equilibrium with arterial blood. The end tidal carbon dioxide tension can therefore, under normal conditions, be measured in place of that in arterial blood, a quicker and simpler procedure. In patients with a tracheotomy end tidal air can be aspirated with a syringe, but in patients without a tracheotomy more complex methods are required, and an electronic infra-red carbon dioxide meter is desirable (Collier and Affeldt, 1954). We have experience of only the simpler method (Walley, 1957).

Chest Radiography.—This is employed in certain cases daily in the acute stage for the recognition of collapse and infection of the lung. Radiographic screening in the convalescent stage allows diaphragmatic weakness to be assessed.

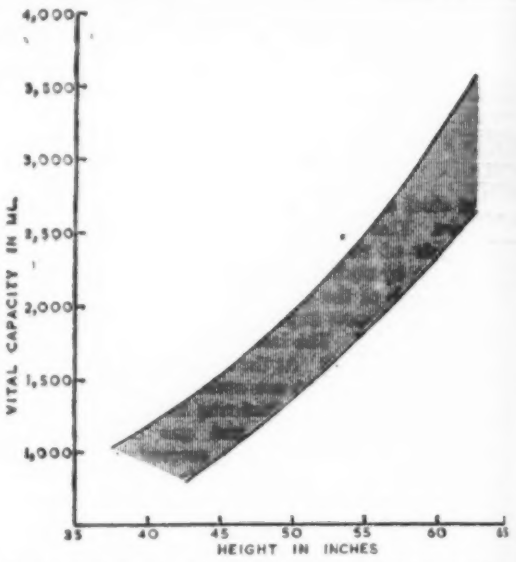
Pressure Measurement.—Respirators used in the treatment of poliomyelitis are always fitted with manometers for the measurement of the pressures being produced. With normal lungs and ventilation in a resting patient the pressures needed are of the order 8–12 cm. of water.

Assessment of Respiration in Practice

The questions to which we have sought an answer are three: (1) Does this patient need artificial respiration and/or measures to clear his airway? (2) When he is receiving assistance, is he being ventilated sufficiently? (3) When he starts breathing on his own, how long can he be expected to breathe at a time, and what is his residual disability?

Need for Assistance

When an adult develops weakness of the respiratory muscles without any weakness of swallowing, ventilation can be assessed by the counting test or, more accurately, by measuring the vital capacity. If these tests are performed on all cases of paralytic poliomyelitis on admission and twice daily, failing ventilation can be detected easily and its speed of development judged. When the vital capacity falls to about a quarter of the predicted normal we usually start respiratory assistance. This is the practice of American workers (Plum, 1952). Normal values for adults are well known. For children down to the age of 5 years we have collected our own figures from measurement of 180 normal convalescents (see Fig.). They agree closely with two British studies (Jones, 1955; Kennedy *et al.*, 1957) and are lower than American figures (Ferris *et al.*, 1952). When the vital capacity falls to this degree the blood gas levels are still normal, or even show evidence of over-ventilation (Dickinson *et al.*, 1953). However, it is important to have the patient confident and co-operative in the tank respirator should the vital capacity continue to fall, as is often the case. Assessment in children below the age of 5 or 6 years is a difficult matter. We have found tracings taken with a face-mask and recording spirometer helpful in a child of 18 months. Rebreathing for a short period increased the tidal air considerably. If there is doubt it is best to artificially respire such children. If they need assistance they will co-operate; if they do not co-operate it is probable that they do not need assistance.



Range of vital capacities of 180 normal convalescent children aged 5½ to 14 years.

In the bulbar case, when swallowing fails, measurement of vital capacity is more difficult, for the presence of secretions in the pharynx appears to inhibit the patient from taking a deep breath. A face-mask must be used in place of a mouthpiece in such cases, for air escapes past the paralysed palate. In fact, the difference between the vital capacity measured with a mask and with a mouthpiece provides a useful test of palatal function in such cases. Partial collapse of the lung may occur in these cases, and this increases the ventilatory requirements and decreases ability. To detect this we make use of routine chest radiography in cases with swallowing weakness. On occasions when other methods give no help, blood gas analysis may provide useful information. The following case illustrates these points.

Case 1.—A girl of 7 years was admitted to hospital with gross pooling in the nasopharynx and so many moist sounds in the chest that pneumonia had been previously diagnosed. She was very restless and quite uncooperative throughout the acute illness. Though treated by postural drainage, a chest radiograph taken on the following day showed segmental collapse of the lung. At this time her chest and arm movements appeared powerful, though her epigastric movement suggested diaphragmatic weakness, and on occasions her colour was poor. To clarify assessment of her respiratory state blood gas analysis was done. This showed an oxygen saturation of 75% and carbon dioxide tension of 60 mm. of mercury. She recovered after tracheotomy and positive-pressure respiration, but she was left with a nasal voice, marked facial weakness, and a diaphragm which radiographic screening showed was very weak.

The possibility of damage to the respiratory centre must be considered in a case of bulbar poliomyelitis. This is difficult to detect with certainty. Irregularity in rate and depth of breathing are the features usually chosen to support this diagnosis (Baker *et al.*, 1950), and

these can be demonstrated with a recording spirometer. But these signs also appear with partial airway obstruction and this is difficult to exclude with certainty. However, if it can be shown that the patient breathes irregularly and develops carbon dioxide retention when unattended but when encouraged breathes regularly and blows off the carbon dioxide, as happened with a case (Sarnoff *et al.*, 1950), then the diagnosis is well established. We have not seen such a combination of events, for signs of peripheral respiratory failure and failure of swallowing have always confused the picture.

Assessment of Artificial Respiration

Radford *et al.* (1954) published a nomogram relating ventilatory requirements of patients at rest in bed to their body weight. Experience at Ham Green has confirmed that ventilation according to this nomogram produces normal blood gas levels in patients whose lungs are normal. The patient who suffers from respiratory weakness alone and can be successfully treated in a tank respirator comes into this category. If the tidal air, measured in these patients with a recording spirometer, is a little more than that predicted by the nomogram, it can be assumed that ventilation is adequate. A more direct method of assessment in these cases is the measurement of end tidal carbon dioxide concentration with an infra-red meter (Collier and Affeldt, 1954). It is possible to use such a meter as part of a servomechanism regulating a tank respirator (Saxton and Myers, 1957). Complexity and expense appear to rule out the routine use of this meter.

Patients who, in addition to respiratory failure, develop weakness of swallowing require a tracheotomy to maintain their airway. Even so treated, they are liable to develop lung collapse and infection, and then require 50–100% more ventilation than predicted by the nomogram. To supply these volumes, pressures of 25–35 cm. of water are needed. In these cases it is necessary to measure oxygen saturation and carbon dioxide tension of arterial blood to obtain a true assessment of respiration (Walley, 1957). End tidal carbon dioxide tension is always below that of arterial blood, and this difference often enables one to diagnose collapse of the lung.

If the arterial blood gas content, end tidal carbon dioxide concentration, and tidal air and inflating pressures are estimated at one time and the chest is radiographed, it is possible to find the ventilation and inflating pressure sufficient to provide normal blood gas levels. So long as routine radiography or clinical observation provides no evidence of changes in the lungs, measurement of the tidal air will then suffice for accurate assessment of respiratory state. In this way two to three blood gas estimations will be enough in the average case. The place of clinical observation lies in the detection of gross changes in the lungs, in oxygen saturation, or in carbon dioxide levels, which threaten life and require immediate action before more precise methods can be used.

Recovery from Respiratory Failure

In many moderately severe cases the vital capacity does not fall below 500–700 ml., figures which are well above the resting tidal air. Such patients can breathe easily on their own when the acute state is over and their temperature falls to normal. Their vital capacity will be found to rise rapidly to double that figure. We have found with others (Affeldt *et al.*, 1957) a qualification which must be made to these statements. Those patients who have marked diaphragmatic paralysis may have greater difficulty with their breathing than might be expected from their vital capacity. The following cases illustrate this point.

Cases 2 and 3.—E. H., aged 24, was left with a vital capacity of 3,700 ml., but became dyspnoeic after slight exertion, while G. M. E., aged 26, with a vital capacity of 2,700 ml., was not dyspnoeic after similar exertion as one would expect. E. H. had marked weakness of the diaphragm, which moved paradoxically when inspiring sharply. E. H.'s functional disability was better illustrated by measurement of his maximum voluntary ventilation and peak expiratory flow. He recorded 48 and 260 litres/min. respectively, while G. M. E. recorded 84 and 310 litres/min.

These case histories also illustrate the value of radiographic screening, and measurement of maximum voluntary ventilation and peak expiratory flow in assessing residual respiratory disability.

With more severely affected patients it is difficult to say how long any one patient may breathe on his own. Measurement of the vital capacity is the only guide we use at present. Others have shown that, with a vital capacity equal to the tidal air, at rest a patient will be able to breathe for periods of from 15 minutes up to a few hours. These and similar figures (Austin *et al.*, 1952; Spencer, 1954; Ferris *et al.*, 1955) we have been able to confirm, but they are general and not particular statements. Ferris *et al.* (1955) have made use of a fall of vital capacity during unassisted breathing as a guide, although we have not found this of much use. Possibly measurement of other function tests may yield useful information; but at present, apart from measurement of vital capacity, we are limited to encouraging the patient to breathe as long as he can while watching for the appearance of any clinical evidence of respiratory distress.

In conclusion it should be mentioned that even a mild upper respiratory infection may set a patient back considerably. For example, the vital capacity of a female patient four months after the onset of poliomyelitis was 2,300 ml. With an upper respiratory infection she became relatively short of breath. Her vital capacity was found to have fallen to 1,300 ml., although no signs were to be heard in the chest and the radiograph was normal.

Summary

The successful treatment of respiratory failure in poliomyelitis calls for an accurate assessment of respiratory function. The methods used in the management of 62 cases of respiratory and bulbar paresis due to poliomyelitis are discussed. The application of these methods to the assessment of the respiratory function of these cases is described.

I thank Dr. J. Macrae for his help and encouragement with the preparation of this paper, which is based on work done with his close collaboration.

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ALTERATIONS IN THE DIURNAL EXCRETION OF ELECTROLYTES DURING INTERMITTENT POSITIVE-PRESSURE RESPIRATION

BY

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The diurnal variations in the excretion of water and electrolytes by the kidney have been studied extensively, the most important contributions to the literature having been listed by Stanbury and Thomson (1951) in an account of their own observations. These authors found the excretion per minute of water and of sodium, potassium, chloride, and bicarbonate ions falls during the night together with the urinary *p*H, whereas the output of ammonia and titratable acid rises. These diurnal excretory rhythms are extremely resistant to attempts to alter their pattern. Thus, starvation, water deprivation for three days, salt deprivation for nine days, the sustained action of deoxycortone acetate and antidiuretic hormone, and the temporary disturbance of the sleep rhythm do not abolish the excretory rhythm (Stanbury and Thomson, 1951).

On the other hand, hyperventilation for periods of 15 to 40 minutes disrupts the excretory rhythm, causing an increased excretion of sodium, potassium, and bicarbonate ions with little change in the excretion of chloride (Brown, Campbell, Elam, Gollan, Hemingway, and Vischer, 1949; Stanbury and Thomson, 1952). This last observation suggests that the nocturnal reduction in the excretion of these electrolytes may be due to the raised alveolar CO_2 tension which develops at night (Mills, 1953). On the other hand, Longson and Mills (1953) found that the maintenance of a raised alveolar CO_2 tension by the inhalation of 5 to 6½% CO_2 for three hours in the morning failed to prevent the matutinal rise in the excretion of electrolytes. Hence, though it is tempting to attribute the variations in the excretory rhythm of electrolytes to changes in respiration, the evidence is at present conflicting.

The maintenance of human subjects on intermittent positive-pressure respiration (I.P.P.R.) for long periods during the treatment of respiratory paralysis has provided an opportunity for further investigation of this problem, the results of which are presented here. This method of artificial respiration permits respiration to be maintained at a constant rate, pressure, and tidal volume by day and by night for long periods; hence the variations in these factors which constantly occur during normal respiration are eliminated. Because patients being thus treated are usually recumbent and variations in the renal excretion of electrolytes during acute changes of posture have been reported (Wilkins, Bradley, and Friedland, 1950), observations on the effects of prolonged recumbency on the diurnal excretory rhythms are reported first.

Material and Methods

Observations on the effects of recumbency were made serially on one subject before, during, and after recumbency, and single observations were made on four other subjects, two of whom were totally paralysed by motor neurone disease, after varying periods of recumbency. The effect of I.P.P.R. was observed in six subjects after varying periods of artificial respiration. The urine was obtained by inserting an indwelling catheter and collecting urine at midnight, 6 a.m., 8 a.m., 10 a.m., 12 noon, 2 p.m., 4 p.m., and 12 midnight. The patients were recumbent and capable of little physical exertion apart from slight movements of the arms. They kept a normal ward routine, sleeping from about 10 p.m. to 6.30 a.m. and taking food by mouth or by nasal tube at the usual meal-times. The respiratory minute-volume was maintained at a level suitable for the patient, and its constancy was checked at frequent intervals throughout the period of collection of urine by passing the expired air through a gas-meter. The sodium and potassium ionic content of the urine was estimated by flame-photometer, and the chloride by a potentiometric method (Sanderson, 1952).

Effect of Recumbency

A male patient aged 28 years with an anxiety state, who complained of intolerable fatigue, was glad to lie recumbent for 21 days. He remained flat in bed, lying on his back, or on either side, but not sitting up. Two estimations, one of which is shown in Fig. 1, were made before he was confined to bed, and showed a normal diurnal pattern for the excretion of sodium, potassium, and chloride. Estimations were made on days 1, 2, 4, 7, 9, 13, and 21 of the recumbent period, but no alteration in the diurnal pattern was observed (Fig. 1). Two further estimations after he resumed activity again showed a normal pattern.

In view of the absence of change with a short period of recumbency, single estimations were made on four other patients. K. T. had disseminated sclerosis and had been in bed for 21 days. D. C. had a prolapsed intervertebral disk, and estimations were made on the 14th and 21st days of recumbency; and J. C. and M. had motor neurone disease and had been in bed and totally paralysed for 17 months and 2 years respectively. All showed normal diurnal excretory patterns (Fig. 2).

Effect of I.P.P.R.

In only two of the six patients on I.P.P.R. was it possible to observe the type of diurnal excretory pattern of electrolytes before treatment was instituted. Both had normal patterns, and, as the remaining four patients

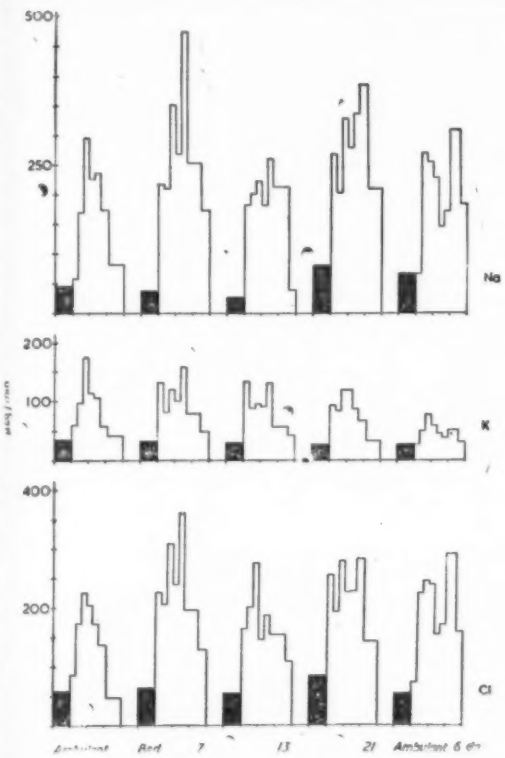

FIG. 1.—Excretion in μEq/min. of Na, K, and Cl in a normal patient before, during, and after a 21-day period of recumbency. Abscissa is marked in six-hour periods starting from midnight, excretion from midnight to 6 a.m. being in black.

were healthy until stricken acutely by a muscle-paralysing disease, there is no reason to believe that they did not have a normal diurnal excretory pattern. J. P., who was on I.P.P.R. for only five days, showed no change in his diurnal excretory pattern. The first change observed in L. S., A. T., C. C., and V. B. was in the excretion of potassium, where a flattening of the tide appeared at a time when the tides of sodium and chloride were unchanged. This is illustrated on the 25th day in C. C., 14th day in L. S., and 21st day in A. T. in Fig 3.

The change was effected by the nocturnal output per minute of potassium rising and the daytime output per minute falling until the excretion per minute was approximately equal by day and by night. The time of onset of this change varied, being present by the seventh day in L. S. and A. T. C. C. was not examined between the 6th and 25th days; the change was present by the latter date and, apart from one narrow peak, there was a suspicion that the change was developing on the sixth day. It was difficult to determine the exact time of appearance of the change in relation to the onset of I.P.P.R. in V. B. because, though the change was present by the third day of continuous treatment, the patient had been treated intermittently over the previous four weeks. In the sixth case, J. C., there was no evidence of flattening of the diurnal excretory pattern of potassium after 28 days' treatment, when I.P.P.R. was discontinued.

The second change in the excretory pattern developed some time later and consisted of a flattening in the chloride tide—illustrated by day 105 in C. C. and by

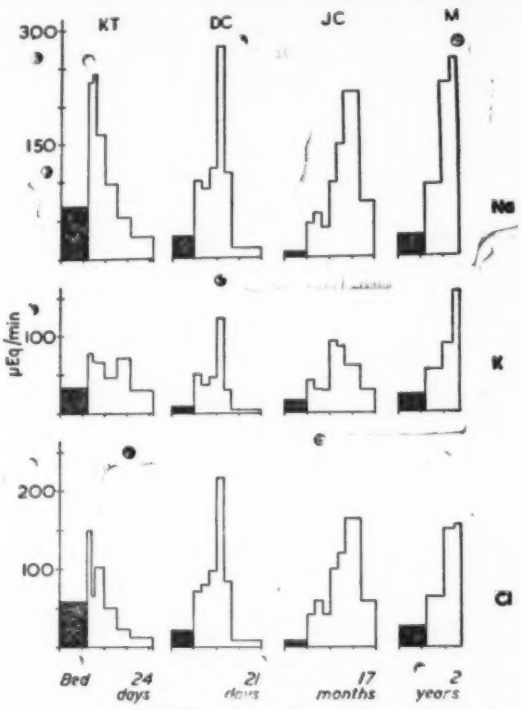

FIG. 2.—Excretion in μEq/min. of Na, K, and Cl in four patients who had been recumbent for varying periods. Scale for D.C. is ×0·5; for M it is ×5.

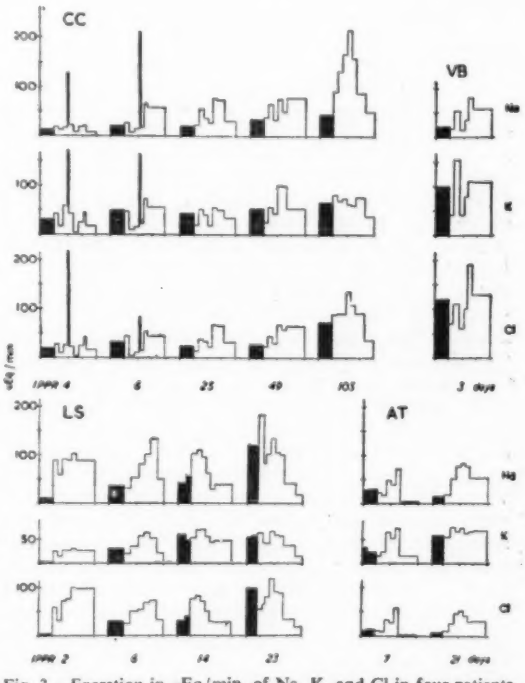

Fig. 3.—Excretion in μEq/min. of Na, K, and Cl in four patients on I.P.P.R. for varying periods. Scales are ×1 except C.C. day 4, Na ×10, Cl ×3; day 6, Na ×10; L.S. day 2, Na ×5, Cl ×5; V.B. day 3, Na and K ×5, Cl ×100; A.T. day 7, K ×5, day 21, K ×3.

day 23 in L. S. (Fig 3). The final change, illustrated by day 23 in L. S., consisted of a flattening in the tide of sodium. The time of onset of the changes in sodium and chloride is hard to ascertain. Both were present by day 23 in L. S. C. C. was not examined between day 105 and day 277, the change in the sodium pattern being present on the latter date.

An important observation in relation to a possible explanation of the change in the diurnal excretory pattern is the total daily output of the various electrolytes. These are set out in the Table, which shows

Total Daily Excretion of Na, K, and Cl in mEq and Serum K in mEq/100 ml. in Four Patients on I.P.P.R.

Patient	Day of I.P.P.R.	Total Daily Output			Serum K
		Na	K	Cl	
C. C.*	4	2·1	48·9	10·4	—
	6	3·6	70·3	53·0	4·2
	25	56·0	57·0	50·0	4·8
	49	81·0	83·0	67·0	—
	105	142·0	92·0	115·0	—
L. S.	2	19·5	27·7	17·7	3·2
	6	90·0	53·0	63·0	3·6
	14	23·5	23·0	23·5	—
	23	135·0	69·0	114·0	4·4
A. T.	7	35·2	8·9	21·3	4·6
	21	49·1	37·4	47·1	—
V. B.	1	21·0	28·0	1·6	4·3

* This patient was receiving supplements of KCl

that at the onset of I.P.P.R. treatment all patients were excreting extremely small amounts of sodium, potassium, and chloride, but later the daily output approached normality. This was probably due to the fact that at the time of induction of I.P.P.R. the patients had become acutely ill and were deficient in both water and electrolytes. These deficiencies were corrected and a rise in the electrolyte excretion followed.

Discussion

The occurrence of diurnal rhythms in bodily functions is not surprising in view of the fact that we are, in general, active by day and at rest by night. One important question is whether these rhythms are inherent in the organism or whether they are determined by external environmental influences. It has in fact been shown that these rhythms are to some degree susceptible to changes in life's routine. Thus Norn (1929) showed that excretory tides were reversed in those who habitually worked by night and slept by day. More recently Lewis and Lobban (1957a) demonstrated in two groups of people living in the Arctic Circle, on 21-hour and 27-hour "days," that the excretory rhythms gradually adapted to the abnormal time routines. The present results in the recumbent patients indicate, however, that variation in physical activity is not the operative factor maintaining or adjusting the rhythms, for the rhythms were clearly present during strict recumbency and even after many months of total paralysis. This does not, of course, prove that the rhythms are inherently determined, for even the totally paralysed patients cannot be regarded as existing under completely basal conditions throughout the 24 hours, for they slept by night and fed by day. It may be that this minimal variation in their daily routine was the sufficient factor for the maintenance of their tides.

When attention is turned to the factors which abolish the tides it is immediately clear from the results with the recumbent patients that the changes in the patients on I.P.P.R. were not due either to their recumbency or to their muscular paralysis. The observations of Evans, Jones, Milne, and Steiner (1954), that potassium depletion abolishes the diurnal excretory rhythm of this electrolyte, makes it also necessary to consider this possibility, especially as patients on I.P.P.R. tend to be hyperventilated and hyperventilation induces potassium loss. The prolonged output of normal amounts of potassium in the urine and the normal serum potassium levels indicate that potassium depletion was not present in the patients, hence it cannot be advanced as the cause of the abolition of the tides.

The fundamental difference between the recumbent and the I.P.P.R. groups was that the former breathed unaided whereas respiration in the latter was controlled with regard to rate, pressure, and tidal volume. Hence it is not unreasonable to suggest that the factor which abolishes the tides is the fixed respiration throughout the 24 hours. How this is achieved is not clear. It could be that fixed respiration acts by its effect on gaseous exchange; on the other hand, it may act by its effect upon pressure relationships within the thorax. Thus Love, Roddie, Rosensweig, and Shanks (1957) have shown that breathing against a rapidly pulsatile pressure increases urine flow and the output of solutes, though breathing against a constant positive pressure had no influence on urine flow or solute output. A further consideration is the observation of Rosenbaum, Ferguson, Davis, and Rossmeisl (1952) that the administration of cortisone abolishes or reverses the excretory tide of potassium and those of sodium, chloride, and water to a less severe degree. It may be, therefore, that fixed respiration acts primarily upon adrenocortical secretion and through this influences the diurnal excretory rhythms. It is not possible to decide among these various possibilities on the basis of the present evidence.

Two further points are worthy of comment. The first is that the tides show great inertia to change. This was noted by Lewis and Lobban (1957a) in their experiments, complete adaptation to abnormal time routines rarely being complete even after six weeks. The present results confirm this, the first change in the potassium tide not being present before at least six days of continuous treatment. This clearly rules out any sudden adjustment of acid-base or intrathoracic pressure relationships as being responsible for the abolition of the tides.

The second point worth comment is that dissociation between the various rhythms undoubtedly occurs. Lewis and Lobban (1957b) observed dissociation between potassium on the one hand and water and chloride on the other hand, the potassium under the conditions of their experiment being the more resistant to change. The present results confirm that dissociation between the various excretory rhythms is possible, though in this instance potassium was the first to change, the chloride and sodium rhythms following later. It is clear, therefore, that different mechanisms are responsible for the various tides.

Summary

The diurnal excretory tides of potassium, sodium, and chloride during periods of recumbency up to two years were unaltered in five patients.

Periods of intermittent positive-pressure respiration of seven days or more flattened first the excretory tide of

potassium in four out of five cases, and later those of sodium and chloride.

Possible mechanisms altering the diurnal tides are discussed.

I wish to thank Mr. J. I. MacNaughton for technical assistance.

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TUBERCULOSIS CONTROL IN DENMARK

BY

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During a recent visit to Denmark I attempted to assess the significance of the differences between the tuberculosis statistics in that country and those in England and Wales.

The decline of tuberculosis in Denmark has been much faster and has gone much further than in England and Wales. This could be due to differences in (*a*) population and environment, (*b*) notification criteria, and (*c*) the actual measures adopted for controlling the disease in the two countries.

General environmental conditions such as diet, housing, rest, and recreation, are equally good in both countries; the long dark winters of Denmark should outweigh on balance the adverse factor of atmospheric pollution in England.

There have been no tuberculous cattle in Denmark since 1951, and the three-yearly routine tuberculin tests performed on all cattle have revealed only an insignificant number of positive reactors infected from human or possibly avian sources.

Denmark is less industrialized than Britain, and has a population of under 4½m. Except in Copenhagen, there is less opportunity for an infected person to pass on his bacilli at work, at play, or when travelling. The Copenhagen incidence rates are actually almost twice as high as the rates for all Denmark and, as shown in the Table, are more comparable with those for the County of Essex.[1] The rates in England vary locally to an even greater extent,[2] the extremes in 1956 being Gateshead with 216 and West Suffolk with 22 per 100,000 of the population.

The keeping of a Central Tuberculosis Register in Denmark does much towards preventing duplication. Each notification is checked at the central register against a list of the tuberculous population, and also against a separate list which is maintained of all names that have been discarded from the register on account of cure, emigration, or inability to examine for three successive years. A double-entry system is used to lessen the chance of duplication due to discrepancies in identification particulars.

New Cases of Respiratory Tuberculosis Notified Annually Per 100,000 of Population

Year	All Denmark	England and Wales	Copenhagen	Essex
1947 ..	85	100	146	98
1948 ..	80	101	154	93
1949 ..	68	102	116	88
1950 ..	58	96	98	87
1951 ..	56	97	82	85
1952 ..	48	95	74	82
1953 ..	40	93	64	72
1954 ..	35	84	66	62
1955 ..	28	76	56	49
1956 ..	25	70	47	49

Relapse is defined as recurrence after freedom from symptoms without treatment for three years or more, and 14% of positive-sputum diagnoses in Denmark in 1955 come into this category. The inadvertent inclusion of such cases in the British incidence figures as new cases could have a considerable effect on the statistics. As the proportion of notifications among the higher age groups increases, so will the chances of duplicate notification increase, since older people are more likely to have had a previous infection, and to have forgotten a notification of long ago, or to have some personal or family reasons for wishing to conceal it.

According to the Danish Tuberculosis Index, less than 3% of tuberculosis deaths had missed notification during life. In England and Wales, however, out of a total of 4,853 deaths from respiratory tuberculosis in 1956, no fewer than 1,244 (26%) are reported as not previously notified.[2] Might not a number of these cases have been notified in another area or under another (for example, maiden) name during life, thus appearing twice in the incidence statistics?

It would obviously be very difficult to maintain a central tuberculosis register for all England and Wales, because of the large population and incidence. Regionalized checking and recording, however, would be more likely to prevent duplication than our present system of accepting notifications from a very large number of local unrelated sources.

When comparing the total known cases of respiratory tuberculosis in the two countries (in 1955) it is found that in England and Wales they represent 691 per 100,000 of the population,[3] but only 6.3% of these were known to be sputum positive at that time; in Denmark the total cases on the registers amounted to only 304.5 per 100,000 of the population, but 25.5% of these were known to be "open" cases, comprising 17.2% with positive sputa and 8.3% with positive stomach washings.

In Denmark about 90% of all notified cases of respiratory tuberculosis are confirmed at some stage by positive bacterial culture, compared with 41% in this country.[3] The bacillus is diligently sought in every case, several sputa and stomach washings being cultured, if necessary. In Copenhagen 30% of the new cases are confirmed by culture of stomach washings, these being cases in which no sputum is obtainable. During 1956 a total of 50,000 sputa and 20,000 stomach washings were sent from all parts of Denmark to the Central Laboratory in Copenhagen for culture, and about 10% of these were positive.

Control of Contacts and Cases

In Copenhagen all patients referred by their doctors, or under surveillance as suspects, contacts, or arrested cases, are seen at the Central Tuberculosis Dispensary. Contacts are examined three times during the first year, twice during the second year, and are discharged three years after the last occurrence of open tuberculosis in the household or work place. Dispensary staff are examined every three months. A full-size picture is taken at the first visit, but subsequently, miniature (70 mm.) film is usually employed, and screening is reserved for difficult or urgent investigations in view of the potential risks of excessive irradiation.

The dispensary doctors are provided daily with details of the hospital bed-state, and have the right to admit immediately. The patient remains in the care of the hospital until treatment is completed, and then is returned to the dispensary for supervision, which continues throughout life.

Mantoux tests are done by the nurses, who also take blood for E.S.R. The tuberculosis nurses are all employed full time as such. For children under 12 the jelly patch test is used, followed by a Mantoux test if positive.

Defaulters are visited by the nurse if an open case is involved; otherwise a letter is sent, and repeated after a month, prior to a home visit being made.

When an infectious patient is removed to hospital or dies at home, the room, bedding, and clothes, are disinfected with formalin by the public health department.

Each patient receives a comprehensive 30-page booklet, *What Every Tuberculous Patient should Know*, and is trained in control measures whilst under treatment. If an open case persists in exposing others to undue risk of infection, and refuses admission to hospital, economic assistance from the State can be withheld. This is usually sufficient to induce full co-operation, but as a last resort the medical officer of health may recommend compulsory removal by the police to hospital or institution, and three or four patients are so dealt with each year in Copenhagen. The case does not go to court unless the patient (already in hospital) complains of unjust detention, and the M.O.H. must then be prepared to prove that a real danger to others actually existed. Husband and wife may not, however, be separated under the above provisions.

Centres for Treatment and Control

Sixty hospitals, sanatoria, etc., are available, with beds at the scale of 0.9 per 1,000 of the population. Most of them are administered by local authorities, but a few by the State through the agency of the National Association for the Fight Against Tuberculosis (N.A.F.T.), which corresponds broadly with our N.A.P.T. (now the Chest and Heart Association).

There are also 102 dispensaries, which are administered by local authorities, and in which 869,000 persons—that is, 20% of the whole population—were examined, and 1,336,430 consultations took place in 1955. During the same year 39,337 B.C.G. vaccinations were done; also 1,016 new cases of tuberculosis were discovered, and over 90% of their household contacts were examined. The dispensaries control the distribution of public and voluntary relief.[4]

In most of the 22 counties, the consultant in charge at the main dispensary is the superintendent of the tuberculosis hospital, and he is also responsible for planning the programme of the mass radiography units throughout the county. This unified control ensures that the special needs of each locality are effectively met and co-ordinated, and eliminates all problems associated with the notification and control of cases discovered by mass radiography.

The fall in the number of cases has led to a great surplus of beds—especially children's beds—in spite of the growing tendency to hold on to non-tuberculous chest cases, which are officially the domain of the general physicians and the general hospitals. Two sanatoria have already been transferred to the Mental Deficiency Hospital Service. It seems probable that the eventual pattern will be a dispensary with a few tuberculosis beds based on each general hospital, and only one or two specializing hospitals retained to serve the whole country for the very chronic homeless and antisocial cases.

Mass Radiography

As in this country, there is a growing feeling in favour of more concentrated attention to selected areas and groups. The areas are, of course, those with a high incidence of tuberculosis; all school staff, Service men, and merchant seamen have annual mass radiography, and in the firms and other organizations which are now well under control after annual radiography for several years attention will in future be concentrated on ensuring *x*-ray examination of all new employees at the time of their appointment, with less frequent examination of the others. Annual examination of the older age groups is being encouraged more actively, also of persons in close contact with the general public—for example, employees in cafés, bars, cinemas, and theatres, bus conductors, hairdressers, dentists, etc. In England and Wales the standard mortality ratio of the above groups is high,[3] so that in addition to having much opportunity to spread infection, they have a high capacity to do so. It is intended to advertise the reasons for selecting a particular area or group in the hope of stimulating response.

Up to now it has been the normal Danish practice to carry out a Mantoux test at the same time as mass radiography, but this is being discontinued in areas where most of the population have already become Mantoux-positive.

Approximately 30% of the population of Copenhagen are now under regular annual survey by virtue of their employment with firms and organizations (including the municipality) which have agreed to adopt this scheme as their general policy. It is popular with the workers, who recognize the protection it affords against risk of contact with an infected person.

Positive findings of active tuberculosis occurred in 0.06% of all persons partaking in mass radiography campaigns in Denmark compared with 0.22% in England and Wales; the figure for Essex was 0.14%. Of all newly notified cases of tuberculosis, 29% are discovered by M.M.R. in Denmark and 21% in England and Wales.

The Danish authorities are very actively dealing with the problem of inter-individual and intra-individual inconsistencies of interpreters of *x*-ray films. In a recent test series, Neilsen,[5] using, with normal chests standard false or "phantom" infiltrates consisting of

aluminium foil *x*-rayed on 70 mm. film, found that the average score of 10 independent readers was 67% of the total number seen by one or more of them. The score of individual readers varied between 41 and 81%. Further studies are now proceeding on the cerebral and sensory factors associated with these subjective variations, and on training methods.

The newer mobile units are equipped with 70 mm. cameras, and all 35 mm. apparatus is gradually being replaced. Public sessions are mostly conducted from school premises and village halls, printed invitations having been sent through the post with an explanatory leaflet to every household in the area.

The films are taken to the Central Copenhagen Dispensary for developing, and are read by two doctors in separate rooms. They start at 8 a.m. daily and are not permitted to use the telephone or receive other messages or distractions until the work is completed. If either doctor queries the film, it is an invariable rule for a full-size picture to be taken.

Three or four days after the *x*-ray examination and Mantoux test the subjects attend again and are told the results. All negative reactors are offered (and accept) vaccination, which is done by the nurses, and a large film is immediately taken if indicated.

The response has been favourable, attendances of between 30 and 80% of those invited having been recorded in different surveys. Since 1946 about one-half of Denmark's population have been examined.

The National Tuberculosis Index is an office which was originally set up to study the future incidence of tuberculosis in classified groups of those who took part in the mass survey of Copenhagen between 1946 and 1948. It has since taken over the statistical analysis of all tuberculosis control measures throughout Denmark. An example of the great value of such an office is the finding that the incidence of tuberculous illness has been significantly higher among unvaccinated persons with a strong Mantoux reaction (12–24 mm.) during a subsequent period of four years' observation, than among all other groups, indicating that they should be frequently and regularly examined.

Prophylaxis

Since 1940 it has been the general policy in Denmark that negative reactors at all ages should be given suspended B.C.G. vaccine. No opportunity of finding non-reactors is missed: infants born in maternity hospitals in Copenhagen (until 1955) were vaccinated before they were 2 weeks old. Many other children are vaccinated at the time of the free medical examination available in the first or second year of life, by their own doctor, under the National Health Service; altogether about 25% of the children in Copenhagen are vaccinated before they enter school. On entry to school (which is at the age of 7 years in Denmark) the jelly patch test is an integral part of the routine medical inspection, and is repeated annually throughout school life in many places, followed by vaccination of non-reactors or revertors. The acceptance rate averages 90%, so that there are very few negative reactors among school children over the age of 8 years. In 1957, 86.6% of all school children in Copenhagen had been vaccinated, and only 8.2% were negative reactors—the rest having converted naturally. As already stated, vaccination is also performed in conjunction with mass radiography.

Up till 1953 B.C.G. was little used in England and Wales, except of contacts and other special groups. The most recent available estimate[3] of the total so far is 653,000. In Denmark, mass vaccination was introduced about 1936, and by the end of 1955 the total number of vaccinations recorded was 1,121,000,[4] and this figure does not include those done privately and in some of the schools. In comparing these figures it must not be forgotten that the Danish population is only one-tenth of ours.

The recommendation to vaccinate all non-reactors has been clear, straightforward, and universal throughout Denmark, without qualifications regarding age or anything else. In many areas consent of parents to the vaccination of children in schools is assumed unless they object in writing as soon as they are informed of the proposed session.

So far as I could ascertain there have been no serious mishaps throughout this long and extensive use of the suspended vaccine. I was impressed by the great care with which it is prepared at the State Serum Institute. Nobody is allowed to enter the laboratory without first washing and changing (in an air-sealed anteroom) into sterile uniform, including cap and mask, from a sealed package. The vaccine is tested for sterility, viability, homogeneity, and *p*H value before issue, and subsequent confirmatory checks on the potency, safety, and allergizing capacity of each batch are done with guinea-pigs. Its reliability to produce allergy has been repeatedly confirmed, and is endorsed by the findings of the Medical Research Council in this country.

There are no signs of a change over to freeze-dried vaccine. It is held that the process of freeze-drying may kill up to 90% of the bacilli, and that faulty suspension, or subsequent exposure, by untrained field workers under adverse conditions, may do further damage. The suspended vaccine is therefore still preferred for general use because of its well-proved potency and safety, though the value of the dried vaccine as a reserve for emergencies is acknowledged.

As regards technique, the Tuberculosis Research Office of W.H.O. has shown[7] that the size of the local reaction increases with the depth of the injection; also that a large local reaction is not necessary for a "good take" as measured by the strength of the tuberculin reaction afterwards. Great care is therefore taken to inject as superficially as possible. The indication given is a diameter of not less than 8 mm. for the weal, which would not be achieved with the standard doses of 0.1 ml. if injected into the deep layers of the skin or subcutaneously. The difficulty of making a very superficial injection without loss of time and leakage from the syringe is well understood; on the other hand, a crop of bad local reactions could make B.C.G. unpopular in a district for a long time.

Whether the size of the subsequent tuberculin reaction and its durability are a true measure of the protection afforded is still uncertain. The only reliable test of this must be the observation of disease incidence in vaccinated and control groups over a number of years. This is being studied by the Medical Research Council in this country,[8] and the incidence rate of primary tuberculosis in the unvaccinated has been about fivefold that in the vaccinated group during the period (two and a half years) of observation so far. More information will be available when morbidity has been

followed up among a parallel series of natural reactors, induced (B.C.G.) reactors, and non-reactors found to be healthy and *x*-ray-negative during the mass radiography surveys in Copenhagen. It will be some years, however, before enough cases of tuberculosis will have occurred among them to enable any firm conclusions to be drawn from this investigation.

It might be appropriate at this stage to consider the arguments on which B.C.G. vaccination has so far been limited in this country to exposed groups and school leavers—namely, (1) that the risk of infection among children is now negligible; (2) that early identification of infected persons through routine Mantoux-testing (by permitting surveillance and prophylactic treatment with isoniazid) presents a more effective method of control than the extensive use of vaccination; and (3) that vaccination of infants and young children has often resulted in severe local reactions and lymphadenitis.

Despite the above arguments, the risk of children becoming infected rises rapidly at school entry, and the rate of natural Mantoux conversion in this country has been estimated at 4% per year of age.[3] In every year since annual mass radiography of school staffs was established in Copenhagen (1949) one or more open cases of tuberculosis have been discovered, and in one year there were as many as seven; in addition, 30 to 40 persons with *x*-ray changes, requiring surveillance, are discovered among them each year. So long as infection of children can occur in school, or is being imported or met when travelling abroad, there is surely a strong case in favour of using a safe means of protection which is known to be 80% effective. Although most natural convertors remain well, the incidence of tuberculous disease among them is nevertheless substantially higher than that among the B.C.G.-converted. Even assuming that reactors can be detected early by routine testing, and that isoniazid prophylaxis is safe and effective, there is no guarantee that the tablets would be swallowed regularly, or that control by this method would be any easier than by mass vaccination. Only in countries where the infection rate among children is known to be high might isoniazid prophylaxis be a suitable alternative to mass vaccination. The Danish authorities are in fact trying this out in Greenland, where over 6% of the population are tuberculous, and most children become tuberculin-positive before it is practicable to offer them vaccination.

The vaccination of newborn infants was suspended in Copenhagen in 1955 because of the frequency of complications. Since then, however, a few cases of tuberculous meningitis and miliary tuberculosis (which had become virtually extinct) have occurred each year, and views are divided on future policy. The Tuberculosis Research Office of W.H.O. has since shown[9] that infants require only one-half to one-quarter the usual dose of B.C.G. to produce Mantoux conversion, and that such doses are much less likely to produce complications. There is little doubt that experience and skill in preventing small amounts of vaccine from getting under the very fine skin of an infant can also reduce this risk.

Mass Education

Propaganda material is used with discrimination in Denmark and is more or less limited to the actual occasions on which vaccination or mass radiography are on offer, when it is delivered to each household by post. Nothing is included which might create fear of the consequences of infection. Response is good and suggests that the Danish population as a whole does not need to be constantly reminded that tuberculosis is an infectious disease. This is in contrast with recent findings in London by David and Chalke, where about 30% of people questioned at random did not think that tuberculosis was infectious.

Control of Cattle and Dairy Products

Tuberculosis has been entirely eliminated from cattle in Denmark by a policy of slaughtering all positive reactors and by strict movement control. Studies carried out during the campaign showed that of 106 tuberculous persons who had been working with markedly tuberculous herds, 59.4% were infected with the bovine type of bacillus, but it is reasonable to assume that this source of cattle infection will decrease with every year that goes by.[10]

The main features of the campaign were: (1) An adequate well-trained staff of veterinary practitioners to ensure biannual testing, examination, and certification of animals and to enlist the co-operation of the farmers. (2) Enlisting the support of the farmers' organizations on an area basis. (3) Adequate State compensation for the slaughter of positive reactors, with extra inducements for prompt action. (4) Compulsory tests and slaughter of reactors in districts with 90% free herds. (5) Medical examination of all cow-hands working with tuberculosis-free herds. (6) Progressive reduction of the selling price of milk produced on farms where segregation of reactors is not practised. (7) Pasteurization of all milk used for feeding stock.

In the beginning the owners of herds with only a small proportion of reactors often decided to get rid of them at once. In herds with more extensive infection, reactors were usually segregated as found, or an attempt was made in some instances to produce a new tuberculosis-free herd by isolating the calves from the adult herd as soon as they were born.

Towards the end of the campaign, progress was swift because the majority of farmers now had clean herds and put pressure on neighbours with infected animals which might reinfect their own; regulations obliged the owners of infected herds to erect an additional fence 2.5 metres inside their boundary fence to minimize the risk of spread to clean herds.

Conclusions

The incidence of tuberculosis has fallen faster and further in Denmark than in England and Wales. This appears to be due to a policy based on the belief that the disease can be entirely eradicated in the reasonably near future, and differing from our own procedures in the following main respects: (1) the maintenance of a Central Tuberculosis Register; (2) intensive examination of sputa and stomach washings in a specialized central laboratory; (3) intensive use of B.C.G. at all ages and in conjunction with mass radiography; (4) selective use of mass radiography, including annual *x*-ray examination of all staff employed in schools, public utilities, etc., as part of their terms of contract; (5) invitations to public mass radiography sessions to individual households by post; (6) wider use of powers for compulsory isolation; (7) unified control.

It would be clearly impracticable to maintain a central tuberculosis register and a central tuberculosis laboratory for the whole of England, but it is suggested that a centre incorporating these services could be established for the area of a regional hospital board, together with selective mass radiography and intensive vaccination under a unified control. Consideration should be given to annual *x*-ray examination as a condition of appointment of school staff and other special categories, and to greater use of existing powers under Section 172 of the Public Health Act, 1936, for the isolation of open cases.

My thanks are due to the Danish Government for a scholarship which enabled me to carry out these studies; to the Essex County Council and the Urban District Councils of Chigwell and Waltham Holy Cross, which, as my employing authorities, generously granted me special leave of absence; and to numerous colleagues, here and in Denmark, who kindly gave me much of their valuable time and facilities for study.

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A HAZARD IN THE USE OF THE BEAVER PULMONARY VENTILATOR

BY

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Recently there have been two potentially dangerous incidents connected with the use of the Beaver ventilator. This communication reports the details and suggests how such incidents may be prevented in the future.

Case Reports

Two patients were suffering from respiratory insufficiency and depression of the laryngeal reflexes. In each case tracheostomy was performed and a cuffed tracheostomy tube inserted. This was connected to a Beaver ventilator in the usual way via the inflating inspiratory-expiratory valve (Mushin, Rendell-Baker, and Thompson, 1959) supplied by the manufacturers.

Progress was satisfactory for several days. Then each patient suddenly became cyanosed immediately following a change of the inspiratory-expiratory valve for cleaning purposes. No cause was apparent, but fortunately the inflating valve was changed for still another. The cyanosis at once disappeared.

Examination of the Valves

In both cases the cyanosis followed immediately after changing the inspiratory-expiratory valve, and on each occasion changing the valve again cured the cyanosis. The suspect valves were carefully dismantled and examined. In both cases the edge of the rubber diaphragm was found to be crinkled and turned over upon itself instead of lying flat. In these circumstances, the flow of air from the ventilator passed straight to the atmosphere and the patient's lungs were not inflated.

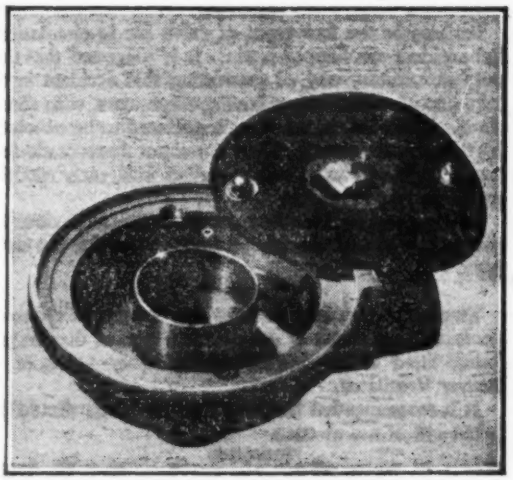

FIG. 1.—Obsolete valve. Diaphragm with short studs.

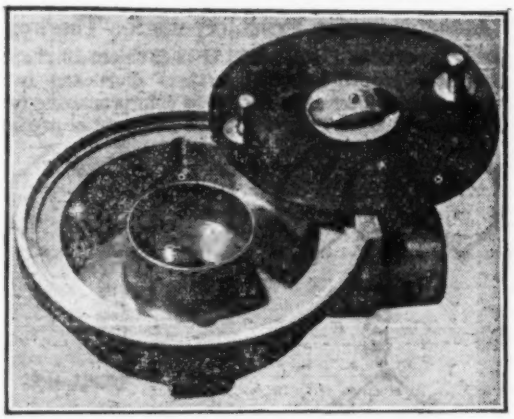

FIG. 2.—Current valve. Diaphragm has long studs.

With the expert assistance of Mr. E. K. Hillard, senior technician to this Department of Anaesthetics, an examination of several other inspiratory-expiratory valves was made. It was found that *two* types of valve were in use. Although outwardly nearly identical, the valves differ internally in one vital detail. In one type, now obsolete but still in circulation, the diaphragm has two large diameter short studs which fit correspondingly large shallow depressions in the valve casing. In the other, the diaphragm has smaller-diameter long studs which fit correspondingly long grooves in the valve casing (Figs. 1 and 2).

Re-examination of the suspect valves showed that a diaphragm with long studs had been placed in a valve-case designed for a diaphragm with short studs. This was an accidental occurence which probably happened when several valves had been cleaned simultaneously.

Prevention

As long as the two types of valve are in circulation the accident can happen again. It is suggested that the only satisfactory way of preventing this accident is to take out of use all valves having diaphragms with short studs. These are, in any case, considered to be obsolete by the manufacturers. They have not been made for some years and were only supplied with early models of the Beaver ventilator.

It is understood that the manufacturers are anxious to exchange, free of charge, all such valves for the new type.

Summary

Two cases are described in which dangerous cyanosis occurred as a result of an obsolete type of diaphragm being fitted to the inspiratory-expiratory valve of a Beaver Ventilator.

It is recommended that the obsolete valves should be taken out of use at once.

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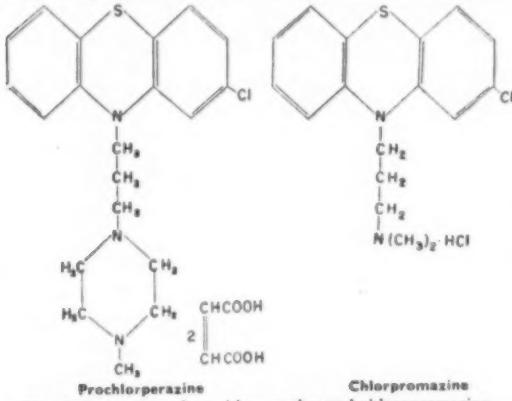
Mushin, W. W., Rendell-Baker, L., and Thompson, P. W., (1959) **Automatic Ventilation of the Lungs,** Blackwell Scientific Publications, Oxford, p. 305.

Jaundice during Prochlorperazine Therapy

Prochlorperazine ("stemetil") (1-[3-(3-chloro-10-phenothiazinyl) propyl]-4-methylpiperazine dimaleate) is a phenothiazine derivative related to chlorpromazine (see Formulae). It has been used in the treatment of psychoneurotic patients (Vischer, 1957), and is an effective antiemetic agent (Smithy and Homburger, 1957). Side-effects that may result from its use are drowsiness, dryness of the mucous membranes, interference with accommodation, Parkinsonism, bizarre neuromuscular disorders, and photosensitive dermatitis (report from May and Baker, Dagenham). There has been no mention in the literature of jaundice following the use of prochlorperazine. We report a case in which jaundice appeared during administration of this drug.



Chemical structure of prochlorperazine and chloropromazine.

Case Report

A 69-year-old man was admitted to hospital on April 3, 1958, with jaundice. He complained of weakness and lethargy for two weeks, during which time he had observed that his urine was dark and his motions were clay-coloured. There was no anorexia, nausea, vomiting, abdominal pain, fever, or weight loss. He had suffered from an anxiety psychoneurosis for many years and had begun treatment with prochlorperazine in November, 1957. He continued taking the drug, approximately 10 mg. daily, until admission to hospital. The total quantity administered was 1,500 mg.

Physical examination revealed a well-nourished jaundiced man. The liver was tender, and was enlarged to 4 cm. below the right costal margin. The liver edge was smooth and regular. The stools were grey and the urine was dark. Examination was otherwise negative. There was no fever.

Laboratory studies disclosed the presence of bile in the urine without increase in urobilinogen. Serum bilirubin was 5 mg. per 100 ml., serum alkaline phosphatase 39 King-Armstrong units, thymol turbidity 0.2 unit, zinc sulphate turbidity 1 unit, serum proteins 8.1 g. per 100 ml. (albumin 5.1 g., globulin 3 g.). Cholecystography and choledochography revealed normal function of the biliary tree without evidence of obstruction to the major bile passages. Examination by barium meal and enema revealed no abnormality. A full blood count showed a haemoglobin value of 13.5 g. per 100 ml., white-cell count 9,200 per c.mm. (neutrophils 5,520, eosinophils 844, lymphocytes 1,548, monocytes 1,196, and band forms 92). A liver biopsy showed no evidence of hepatocellular damage. There was occasional bile plugging of canaliculi.

Prochlorperazine was suspended on admission to hospital, and during the subsequent two weeks the patient's jaundice subsided. At this time serum bilirubin was 1 mg. per 100 ml. and the serum alkaline phosphatase 23 King-Armstrong units; thymol turbidity 0.2 unit, zinc sulphate turbidity 1.1 units, serum proteins 7.1 g. per 100 ml. (albumin 4.5 g., globulin 2.6 g.). The eosinophil count had returned to normal. Follow-up liver-function tests and full blood counts performed three months later were within normal limits.

Comment

This patient received prochlorperazine for four months as an ataractic agent, the total dose being 1,500 mg. There was no history of exposure to other recognizable hepatotoxic agents or drugs. He developed an obstructive type of jaundice, with a raised serum alkaline phosphatase level; hepatocellular function tests were normal. There was also a transient eosinophilia. Liver biopsy revealed no evidence of parenchymal injury. On withdrawal of the drug the jaundice subsided. Jaundice is known occasionally to follow the administration of chlorpromazine (Lemire and Mitchell, 1954; Zatuchni and Miller, 1954; Hartnett, 1955), and Hubble (1941) has reported the hepatotoxic action of phenothiazine.

Prochlorperazine is chemically related to chlorpromazine and promazine, and shares a common phenothiazine group. Prochlorperazine would also appear to share with these drugs the propensity to induce jaundice.

We thank Dr. W. Freeborn, general medical superintendent, of the Royal North Shore Hospital of Sydney, for permission to publish this paper; and Dr. C. Graham for reviewing the histopathology.

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Reviews

ON TUMOURS OF THE BREAST

Treatment of Breast Tumours. By Robert S. Pollack, M.D., F.A.C.S. (Pp. 147; illustrated. 45s.) London: Henry Kimpton. 1958.

This American publication is a most expensively produced and beautifully illustrated account of the pathology and treatment of breast tumours by a group of workers in San Francisco, mostly from Stanford University, where the principal author and editor is clinical instructor in surgery.

In the chapter on pathology malignant growths are divided into those of ductal origin and those of glandular origin, a distinction which would not recommend itself to the majority of British pathologists. The technique of removal of a benign tumour is described in detail with copious illustrations. This operation, often neglected in textbooks on operative surgery, is sometimes rather badly done, and it is a pleasure to find that its execution is regarded as a matter of some importance. The medical treatment of "chronic mastitis" which is recommended is somewhat unusual and no evidence is adduced that it has any effect. Other chapters relate to the primary treatment of early breast cancer, surgical techniques for simple and modified mastectomies, and the common problems related thereto. The extended radical mastectomy is described, but praiseworthy caution is enjoined in formulating indications for this operation. Radiotherapy and the various treatments depending upon hormonal dependence receive due attention.

This is a book which might take a modest place in the library of a surgeon especially interested in diseases of the breast.

HEDLEY ATKINS.

ESSAYS BY VIRCHOW

Disease, Life, and Man. Selected Essays by Rudolf Virchow. Translated and with an introduction by Lelland J. Rather. (Pp. 273+viii. 32s 6d.) Stanford: University Press. London: Oxford University Press. 1959.

This book is a translation of ten essays by Rudolph Virchow, the first written when he was a young man of 26, the last at the age of 77. Professor Rather has added an introductory essay contrasting the methods of Virchow with those of Harvey and Claude Bernard. It would have been interesting to have had a little more biographical detail of Virchow himself, for he was a man of many parts; but Professor Rather has provided condensed notes on many of the personalities mentioned in the essays, which add to their interest.

The essays cover a period of the nineteenth century (1847–98) and provide a fascinating and worthwhile survey of the changes in outlook during that period. When Virchow wrote the first essay medicine was at the point of emergence from "natural philosophical" and "natural historical" bounds, and the gap between physiological and practical medicine was wide. Virchow urged the need for careful detailed investigations, the right use of hypothesis, and the study of pathology by a physiological approach and by experiment. These ideas found expression in his teaching and emphasis on cellular pathology, which is the central theme of most of the essays.

Throughout the book there are investigating glimpses of Virchow's contemporaries, on whom his views are sometimes more forcefully than politely expressed. In the essay "One Hundred Years of General Pathology" we have a fascinating pen picture of some of the practitioners of pathology in the nineteenth century, and inevitably something of Virchow's own personality becomes apparent to the reader.

This, unlike many collections of essays, is rather more than light reading for the occasional half hour.

IAN DAWSON.

PHILOBATISM AND OCNOPHILIA

Thrills and Regressions. By Michael Balint, M.D., Ph.D., M.Sc. With a chapter on "Distance in Space and Time," by Enid Balint, B.Sc. (Pp. 147. 18s.) London: Hogarth Press. 1959.

This book is volume No. 54 in the International Psycho-Analytical Library, a series well known for its mumpsimus qualities. The present volume is no exception in this respect. It purports to present a new typology, consisting of philobatism and ocnophilia, two types which have obvious relationships to extraversion and introversion. Balint dismisses Jung's and Kretschmer's typologies as being "descriptive rather than dynamic classifications, useful while discussing people but not really helpful when trying to treat them." There is no evidence in this book that the new concepts are any more useful in treatment, and in any case Jung and Kretschmer would probably consider their own types at least as "dynamic" as Balint's. Indeed, as the term is quite undefined it does not seem to carry very much meaning.

In establishing the existence of his types Balint very carefully refrains from making use of any of the advances in psychological methodology achieved in the last fifty years; his discussion bears a distinct similarity to the type of character description so well done by the Ancient Greeks. Reliance is entirely on argument, ancedote, and a rather superficial kind of semantic analysis of the origins of certain words; there is no reference to controlled observations of people, and only very casual references to case studies. The style is turgid and the organization of the material poor; the author seems to have been incapable of following one train of thought through without hunting after every hare stirred up in the process. Altogether this book can hardly be regarded as a serious contribution to either medicine or science.

H. J. EYSENCK.

BOOKS RECEIVED

Air Ministry Handbook of Preventive Medicine. 2nd ed. (Pp. 418+xxix; illustrated. 40s.) London: Her Majesty's Stationery Office. 1959.

Modern Science and the Human Fertility Problem. By Richard L. Meier. (Pp. 263+xiii. 48s.) New York: John Wiley and Sons Inc. London: Chapman and Hall. 1959.

Eighth Congress of the Universities of the Commonwealth 1958. Report of Proceedings, Montreal, September 1-5. (Pp. 99+xxix. 12s. 6d.) London: Association of Universities of the British Commonwealth. 1959.

Sulfur in Proteins. Proceedings of a Symposium held at Falmouth, Massachusetts, May 1958. Organized and edited by Reinhold Benesch, Ruth E. Benesch, Paul D. Boyer, Irving M. Klotz, W. Robert Middlebrook, Andrew G. Szent-Györgyi, and David R. Schwarz. (Pp. 469+xi; illustrated. $14.) New York and London: Academic Press Inc. 1959.

BRITISH MEDICAL JOURNAL

LONDON

SATURDAY JULY 25 1959

INSTALLATION OF THE PRESIDENT

Because the Duke of Edinburgh was still in Canada during the Joint Annual Meeting of the British and Canadian Medical Associations in Edinburgh, his installation as President of the British Medical Association has been postponed until the autumn. The ceremony will take place in B.M.A. House on October 28, and in the evening the Duke will be present at the Council dinner of the Association. Before he left for Canada the Duke of Edinburgh recorded a message to be read at the Adjourned Annual General Meeting of the Association in Edinburgh on July 20. This is reproduced below.

"When I accepted your invitation to become President of the British and Canadian Medical Associations, I had every intention to be present at the Joint Meeting in Edinburgh. However, as I am sure you know only too well, nothing in this life is entirely certain, and I am at present in Canada due to circumstances quite beyond my control.

"I am particularly sad not to be with you, because this meeting of British and Canadian medical men is just that kind of Commonwealth co-operation which can do the most good. The meeting together of men of like minds, working to the same end, demonstrates the value of the Commonwealth connection and uses it to achieve practical results.

"Although I have to miss the Joint Meeting in Edinburgh, I have had the privilege of being installed as President of the Canadian Medical Association in Toronto only a short while ago. This was a most pleasant and successful affair, which I am sure my Deputy President, Dr. Kirk Lyon, will confirm. Later this year I look forward to my installation as President of the British Medical Association. As I understand that it is customary for the President to deliver a short address on that occasion, I do not propose to anticipate that task to-day.

"This is simply a short message of apology and encouragement in my unavoidable but still regrettable absence. I hope very much that you will all enjoy the present meeting and that the arguments will be fierce and long. There is no better way to find out the strength of opinions and ideas than open and unfettered discussion. It is also my hope that the whole meeting will take place in a happy and co-operative atmosphere, because it is bound to colour the outlook of all those who are attending for the next 12 months and, speaking as a customer, I would rather be attended by someone who had been inspired by happy and lively conference than depressed by a series of dull debates.

"I wish the meeting every success."

KEEPING UP WITH THE KININS

The hormones of the posterior lobe of the pituitary gland, oxytocin and vasopressin, are now known to be polypeptides. Several other substances have been extracted from living tissues and fluids, substances which like oxytocin and vasopressin are also physiologically active polypeptides. The common property which gives them the name of kinins is that they cause contraction in smooth muscle. In the last few years the number of these substances being discovered has increased at an alarming rate. Each appeared to be different from the others, and it seemed as if Nature was going to make it impossible for the pharmacologist to reduce them to any kind of order. The most recent evidence, however, indicates that several of them are identical.

One of the earliest kinins was substance P found by U. S. von Euler and J. H. Gaddum[1] in alcoholic extracts of brain and of intestine. Another was bradykinin, which Rocha e Silva and colleagues[2] obtained by incubating plasma or serum or globulin with the venom of the snake, *Bothrops jararaca*. Most of the kinins have indeed been obtained by the splitting of serum protein by an enzyme, with the resulting liberation of a polypeptide which is physiologically active. Another was kallidin, which became known through the work of E. K. Frey and colleagues.[3] They originally extracted a material which they called kallikrein from several tissues and body fluids. This substance caused a fall of blood pressure and resembled an enzyme. E. Werle[4] observed that when kallikrein came in contact with blood proteins a second substance was formed, not a protein, but having a smaller molecule, which they called kallidin. To-day we know that bradykinin and kallidin are the same substance, and the properties previously attributed to kallikrein now are attributed largely to kallidin.

Another kinin is plasma kinin, which has been studied by G. P. Lewis.[5] There is in blood an inactive precursor, plasminogen, of a proteolytic enzyme plasmin. When plasminogen is activated and plasmin is set free, the plasmin splits off the plasma kinin from the blood proteins. This substance is now known to be identical with bradykinin and kallidin. The same plasma kinin is formed when saliva acts on blood proteins, and it is responsible for the functional hyperaemia in the gland which accompanies salivary secretion. It is interesting that here we have a relation between the action of human saliva and that of snake venom.

Then D. Armstrong and colleagues[6] observed that when fresh plasma came in contact with glass it developed activity like that of plasma kinin, stimulating smooth muscle and causing vasodilatation. Under these conditions a substance which caused pain when applied to the base of a blister was produced as well. The pain-causing substance has been shown to be similar to bradykinin.

The probability is high that kinins occur normally in the body and that they have a physiological role—as, for example, in maintaining a vigorous flow of

[1] Von Euler, U. S., and Gaddum, J. H., *J. Physiol.* (*Lond.*), 1931, **72**, 74.
[2] Rocha e Silva, M., Beraldo, W. T., and Rosenfeld, G., *Amer. J. Physiol.*, 1949, **156**, 261.
[3] Frey, E. K., Kraut, H., and Werle, E. *Kallikrein* (*Padutin*), 1950, Stuttgart.
[4] Werle, E., *Biochem. Z.*, 1937, **289**, 217.
[5] Lewis, G. P., *J. Physiol.* (*Lond.*), 1958, **140**, 285.
[6] Armstrong, D., Jopson, J. B., Keele, C. A., and Stewart, J. W., ibid., 1957, **138**, 350.
Gaddum, J. H., and Horton, E. W., *Brit. J. Pharmacol.*, 1959, **14**, 171.
[6] Schachter, M., and Thain, E. M., ibid., 1954, **9**, 352.

blood through the salivary gland during secretion. When tissues are damaged it is likely that the activator streptokinase is set free which converts plasminogen into plasmin, this in turn giving rise to plasma kinin. The plasma kinin will increase the blood flow at the site of injury. Such plasma kinin is excreted in the urine, for recently J. H. Gaddum and E. W. Horton[7] have examined a kinin present in urine, and have found that it could not be distinguished from kallidin or from bradykinin. It therefore looks as though bradykinin, plasma kinin, kallidin, pain-producing substance, glass-activated kinin, and urinary kinin will turn out to be one and the same thing. The only kinin which is different seems to be wasp kinin, described by M. Schachter and E. M. Thain,[8] which is distinguished from the others by the fact that it is not destroyed by crystalline trypsin. Wasp kinin deserves attention, for it is responsible for the prolonged oedema which often follows a wasp sting.

ANNUAL CLINICAL MEETING

The Association's second Annual Clinical Meeting will be held at Norwich from the evening of Thursday, October 22, to midday on Sunday, October 25, at the invitation of the Norwich Division. Judging by the success of last year's meeting at Southampton, and the excellence of the Norwich programme, a large attendance of doctors can be expected. To help in the arrangements, those proposing to go there are asked to notify the Executive Officer, Norwich Meeting, at B.M.A. House, as early as possible.

As befits the title and purpose of the meeting, the emphasis throughout is on practical medicine. After a Civic Reception by the Mayor and Corporation of Norwich on the first evening, there follow two days loaded with rich clinical fare. Each morning begins with a general session at which invited speakers will talk on such topics of the moment as "The New Penicillins," "Indications for Therapeutic Abortion," and "The Therapeutic Applications of Radio-iodine." Then comes a symposium: on Friday a team of experts will discuss "Anticoagulants" and on Saturday another team will debate the problem of "Hospital Infection." To complete the morning sessions there is live colour television of surgical operations at the Norfolk and Norwich Hospital. Immediately after lunch there are films. Then on Friday afternoon an extensive series of clinical demonstrations will be given at the Norfolk and Norwich Hospital by the staff. These will cover not only general medicine and surgery and obstetrics but most of the clinical specialties also, including, for instance, geriatrics and paediatrics.

On Saturday afternoon there will be a choice of three panel discussions—on "Tetanus," "The Obese Child," and "Head Injuries" respectively—followed by the *chef d'oeuvre*, a Transatlantic Clinical Conference on gastro-intestinal cases. The cases will be discussed over the Transatlantic cable by a team of American doctors in Philadelphia and by a British team in Norwich consisting of Professor L. J. Witts, Mr. Harold Edwards, and Dr. F. H. Kemp, with Dr. W. A. Bourne as moderator. The meeting is rounded off with a programme of social events which include an Italian play at the famous Maddermarket Theatre, a lecture tour of the City Art Gallery, and a reception by the Norwich Division. The local officers at Norwich, notably the honorary secretaries, Dr. R. H. Scott and Dr. A. Batty Shaw, have worked strenuously to make the meeting a success. Those who take part can be assured of an instructive, friendly, and thoroughly worthwhile three days.

INHIBITION OF LACTATION

It is now generally agreed that the purpose of giving hormones in the inhibition of lactation is to prevent the breast engorgement and pain which otherwise are the consequences of the absence of suckling—itself the cause of inhibition of milk secretion. Oestrogens by mouth have been most widely used, but large doses, not always well tolerated, are required, and a clinically satisfactory result is by no means invariable. It is of interest, therefore, that a single injection of a combination of long-acting esters of androgen and oestrogen has been fairly extensively tested as a method of preventing breast engorgement when breast-feeding is not to occur, and has given good results. The preparation used, called "deladumone" in the U.S.A. (the equivalent in this country is called "primodian depot"), contains testosterone oenanthate 90 mg. and oestradiol valerate 4 mg. per ml.

The first report on the use of deladumone for this purpose was by W. W. Stein,[1] who treated a total of 253 patients, each of whom received a single intramuscular injection immediately after the third stage of labour. He first tried varying doses and found that 3.5 ml. was the most effective one. Of the 136 patients who received the full dose, 77% had complete absence of breast engorgement, lactation, and discomfort, 84% had no engorgement, 81% no lactation, and 91% no pain. In three cases the onset of symptoms was delayed until the 13th post-partum day. In none of the successful cases did breast symptoms recur later. Two further reports add evidence of the efficacy of this treatment, which was found to be most effective when the injection was given in a dose of 3 or 4 ml. at the end of the first stage of labour or within the first hour after delivery. J. B. Watrous, R. E. Ahearn, and M. A. Carvalho[2] found an incidence of breast engorgement of 69% in 42 control patients who received no hormones, but an incidence of only 8.3% in 268 patients who were treated with hormones. Some of those who were given a mixed androgen-oestrogen preparation by mouth developed breast engorgement later on; none of those who received deladumone by injection did so. However, too small a dose of deladumone or too great a delay in administering it much reduced its effectiveness. In the series of 197 patients treated by B. Lo Presto and E. Y. Caypinar,[3] the most effective procedure was again found to be an injection after the first stage of labour. Out of 47 patients given 3 ml. of deladumone at that time, 43 remained completely asymptomatic. There was no evidence of interference with the course of labour or of the puerperium, or of abnormal bleeding or masculinization. It is also interesting to note, in support of the opening sentence of this annotation, that three women who changed their minds after they had received their injections and wished to breast-feed their infants had no difficulty in doing so.

[1] Stein, W. W., *Amer. J. Obstet. Gynec.*, 1958, **76**, 108.
[2] Watrous, J. B., Ahearn, R. E., and Carvalho, M. A., *J. Amer. med. Ass.*, 1959, **169**, 126.
[3] Lo Presto, B., and Caypinar, E. Y., ibid., 1959, **169**, 130.

Correspondence

Radioiodine in Thyrotoxicosis

SIR,—Your leading article on radioiodine in the treatment of thyrotoxicosis (*Journal*, June 20, p. 1578) emphasizes that it is still too early to make a definite statement on the carcinogenic potency of 131I in humans. It is, however, surprising that you do not mention the occurrence of cases of leukaemia following such therapy, and the important question of whether such cases are likely to be fortuitous or induced by the treatment. Particulars of eight cases have been published[1-8] and I know of two further unpublished cases. The leukaemia was described as acute in all of the nine cases for which I have particulars, and developed at about 18 months after radioiodine treatment in six of them, occurring after 2, two and a half, and 7 years in the other three.

In view of the large number—tens of thousands—of patients, many of them elderly, that have been treated in this way during the last 15 years it is to be expected that some would have developed leukaemia even if not so treated. A provisional estimate, which is at present under review, suggests that from 5 to 10 cases might have been expected on a chance basis, although the observed frequency of acute leukaemia occurring at about 18 months after treatment makes a fortuitous origin of all the recorded cases appear somewhat unlikely. At the same time, even if all of the 10 cases were ascribable to the treatment, we should still have no evidence that leukaemia was more than a rare sequal, with an incidence substantially under 0.1 per cent. in the periods of follow-up at present available.

It is clearly important, however, that any cases of leukaemia following radioiodine treatment should be recorded; and that estimates should be obtained of the number of such cases to be expected by chance, and of any additional incidence that may be attributable to the treatment.—I am, etc.,

E. ERIC POCIN.

M.R.C. Department of Clinical Research,
University College Hospital Medical School,
London, W.C.1.

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2 Abbatt, J. D., Farran, H. E. A., and Greene, R., **Lancet**, 1956, **1**, 782.
3 **Argonne Cancer Research Hospital, Proceedings of the Conference on Radioiodine, November 1956 (ACRH-100)**, p. 33, line 15.
4 ibid., line 9.
5 Werner, S. C., and Quimby, E. H., **J. Amer. Med. Ass.**, 1957, **165**, 1558.
6 Blomfield, G. W., Eckert, H. Fisher, M., Miller, H., Munro, D. S., and Wilson, G. M., **Brit. med. J.**, 1959, **1**, 63.
260, 76.
7 Vetter, H., and Hofer, R., **Brit. J. Radiol.**, 1959, **32**, 263.
8 Kennedy, W. M., and Fish, R. G., **New Engl. J. Med.**, 1959,

"Tofranil"

SIR,—There is a rising tide of so-called thymoleptic drugs in the treatment of psychiatric disorders which, now that they have become available to the general practitioner, might become a tidal wave. That there are attendant risks in the use of these potent drugs has been amply demonstrated by articles and letters in the medical press some of which are not mentioned, or inadequately so, in the literature of the manufacturers. We feel obliged, therefore, to call attention to a complication in the use of one of these drugs—"tofranil"—to which only scant reference has been made, i.e. the transformation of a chronic depressive state into one of hypomania.

We have used tofranil in sixteen cases of chronic depression with positive results in seven cases. In two of these cases, however, a hypomanic state was precipitated which has not subsided in spite of the withdrawal of the drug for three weeks in one case and four weeks in the other. It must be emphasized that in neither case has there been a previous manic swing.—We are, etc.,

Horton Hospital, Epsom, Surrey. HENRY R. ROLLIN.
E. L. UDWIN.

Cracked Foreskin

SIR,—With reference to the letter by Dr. Kenneth Bhagan in your issue of April 18 (p. 1046) I would like to state my experience of three cases of diabetes who had cracks on the foreskin. All were overweight Hindus, past 50 years of age. The first case was in a known diabetic who developed painful cracks on the foreskin, which improved only when his diabetes was controlled. The other two cases presented with cracks as the only symptom. The experience of the first case prompted urine testing which revealed the presence of diabetes. Here also control of the diabetic state resulted in healing of the cracks.

In addition to pain, the patients also complained of itching sensation. It appears that diabetes is responsible for this condition.—I am, etc.,

Ahmednagar. D. B. LELE.

Antimalarials in Sjögren's Syndrome

SIR,—I have read Dr. J. M. Heaton's paper (*Journal*, June, 13, p. 1512) with great interest. His 25 patients were middle-aged and elderly females, and two-thirds had arthritis. Sjögren himself found arthritis in 80% of his cases. The lesions associated with the syndrome affect the mesoderm mainly—skin and mucosa changes being trophic and secondary to periarterial and perineural round cell infiltrations[1]. Periarteritis, enlargement of spleen and lymph nodes, anaemia, and a high rate of red cell sedimentation are common just as in rheumatoid arthritis and collagen disorders. Vitamin deficiency and infection seem to play no part in its aetiology. There is much evidence that Sjögren's syndrome is yet another variant of the rheumatoid arthritis group which include Felty's syndrome, Still's disease, and possibly Reiter's syndrome, and that its mesodermal lesions are those of a chronic hypersensitivity state.

It is, therefore, not surprising that Sjögren's syndrome should respond to chloroquine and to hydroxychloroquine in the same way as many other hypersensitivity states and rheumatoid arthritis benefit[2,3]. I would be interested to know whether Dr. Heaton's failure in six cases of his series concerned patients with normal red cell sedimentation rates. In my experience it is useless to exhibit antimalarials in rheumatoid arthritic patients with normal sedimentation rates even if the clinical picture suggests active lesions. Dr. Heaton mentioned that 4-8 weeks of treatment may elapse before a beneficial response can be expected, which confirms observations in rheumatoid arthritis. It is important to impress upon patients that effects of chloroquine and hydroxylchloroquine cannot be expected before four weeks of

high dosage therapy. Lastly I would suggest that treatment of Sjögren's syndrome and of rheumatoid arthritis and allied conditions be continued for no less than 18 months, that high doses should be given for at least four months, and that the maintenance dose be no less than 300mg. chloroquine base or 400mg. hydroxylchloroquine.—I am, etc.,

Liverpool, 1 H. FULD.

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2 Fuld, H., ibid, 1958, 14, 12.
3 Fuld, H., and Horwich, L., Brit. Med. J., 1958, 2, 1199.

Acroparaesthesia and the Carpal Tunnel

SIR,—Your interesting leading article (*Journal*, May 9, p. 1230) on the carpal tunnel syndrome would seem to imply that the symptoms of acroparaesthesia are produced by ischaemia of a localized segment of the median nerve due to occlusion of the neural vessels by the pressure of the flexor ratinaculum. Although this explanation appears to be supported by ischaemic compression tests and would at first seem to explain the immediate relief obtained by division of the ligament, I do not believe that a segment of a peripheral nerve can be intermittently deprived of its arterial blood supply by any slowly developing compression mechanism. Blunt and Stratton's work[1] demonstrating the capacity of the neural intrinsic longitudinal vessels to compensate for the ligature of segmental vessels, suggests that an adequate collateral circulation is available to prevent local ischaemia of nerve fibres under the degree of compression which can occur beneath the carpal ligament.

Recent observation at operation has suggested a different explanation for the cause of the paraesthesiae. I have noticed in many cases a row of longitudinally arranged vessels in the segment of nerve beneath the carpal ligament. Gentle dissection of the nerve shows that these vessels are present throughout the interior of the nerve as well as on its surface. They are probably identical with the "flush" reaction referred to by Wiley[2]. They fill from their distal end and are venous in nature, pervading the nerve in a segment mainly distal to the tightest part of the ligament. This localized area of venous congestion in the nerve seems to develop as a result of the gradual obstruction of the venous channels by the carpal ligament. It is unlikely that movement of the fingers and use of the hand during the day can keep the blood flowing through the nerve, but at night, when hand and finger movement ceases, venous blood will stagnate in these enlarged veins and local tissue changes will directly affect the sensory nerve fibres with production of paraesthesiae. The time interval between getting off to sleep and awakening with symptoms allows gradual stagnation of blood to occur in the hand and affected segment of nerve, and the gradual building up of tissue metabolites. On waking with pain and paraesthesiae in the hand, relief is obtained by the characteristic rapid finger movement, shaking the hand and fingers, massage and elevation of the hand—all actions which assist emptying of the congested nerve. Division of the carpal ligament allows the normal venous flow to be re-established with immediate and permanent relief of symptoms.—I am, etc.,

Liverpool GEOFFREY OSBORNE.

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2 Wiley, A. M., Postgrad. Med. J., 1959, 35, 30.

Tobacco Amblyopia

SIR,—May I add to your annotation on tobacco amblyopia (*Journal*, June 20, p. 1582) a note that the "latent period of about four to six weeks" before any improvement is to be expected after genuine cessation of use of tobacco in any form may *occasionally* (especially in the more elderly patient) be protracted for as long as a year, yet with ultimate recovery of full normal visual acuity?

Such unusual delay in diminution of the depth of bilateral centrocaecal scotomata may lead the G.P. and consultant to question the accuracy of the diagnosis (which should certainly be reconsidered), but need not cause undue despondency in the absence of signs of progressive optic atrophy. Suspicions of the patient's protestations of total abstinence are sometimes, but not always, justified.—I am, etc.,

Hull. D. D. STENHOUSE STEWART

B.C.G. Vaccination

SIR,—One of the authors of the article entitled "The Case Against B.C.G." (*Journal*, June 6, p. 1423) is Professor J. A. Myers, who as early as 1940 wrote a book entitled *Man's Greatest Victory over Tuberculosis*[1]. It is a well written book of 419 pages almost solely dedicated to the assertion that there is no way of distinguishing in the laboratory between human and bovine tuberculosis, and that in consequence the surest and quickest method of overcoming human tuberculosis would be the eradication of tuberculosis in cattle. In 1940 bovine tuberculosis was still very common in this country, but we have been told that it will have been eradicated in most countries by 1960. Nobody wants to belittle the great success of our veterinary colleagues, but most medical men in this country think, I am sure, that modern chemotherapy and thoracic surgery have contributed at least as much as veterinary medicine to our, still only partial, victory over tuberculosis.

I was puzzled by the figures quoted in the paper by Dr. Arnold S. Anderson and his colleagues. In one instance (top of page 1424) the percentage of positive reactors to tuberculin among junior high-school students in 1957/57 was reported as reaching only 3.7 per cent. By contrast, we read on page 1426 that among 6,823 children of 6-14 years of age, observed over a period of 20 years, beginning in 1921, there were 2,979 children who reacted to tuberculin[2]. The percentage in this investigation, presumably ended in 1941, would amount to 43.6 per cent (!) of positive reactors and this among children from 6-14 years of age.

In conclusion, neither veterinary experience nor the published figures seem to me to give definite evidence in favour of the arguments about "The Case against B.C.G."—I am, etc.,

Brockley, London, S.E.4. ARTHUR E. SELEGMANN.

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SIR,—A scheme of B.C.G. vaccination of schoolchildren aged between 13 and 14 years was introduced in Barking during the autumn term, 1954, and has operated since that time. Both the Heaf and Mantoux tests were performed simultaneously in the pre-va...

tion tuberculin sensitivity testing of all the children, and the results obtained are compared below:

Year	Number Tested	Total No. of Reactors	Heaf Test	Mantoux Test
			Positive Results	Positive Results
1954	214	23	23	22
1955	675	96	96	86
1956	751	97	93	97
1957	863	71	70	71
1958	723	75	75	73

These results indicate close agreement (97%) between the two methods, and, in view of the ease and simplicity of operation particularly with the self-firing apparatus now available, we have decided to rely in future on the Heaf test for mass skin-testing in this connexion.—I am, etc.,

F. GROARKE.

Public Health Department,
Barking, Essex.

"Disipal"

SIR,—I would very much like to support Dr. R. O. Gillhespy's letter (*Journal*, April 25, p. 1119). Certain other effects have come to light during the course of treating 38 patients here with "disipal" (benzhexol hydrochloride). It has been found to be very effective in removing depression and has also acted as a detensor. I think that this effect has been quite marked with patients suffering from Parkinson's disease, and it has also been effective in cases who have suffered from reactive depression in whom there is some agitation and tension. Of 38 unselected cases which we have treated with disipal, 63% showed marked improvement. I hope to send you a fuller report in due course.—I am, etc.,

GLYN DAVIES.

Bowden House,
Middlesex.

Aetiology of Disseminated Sclerosis

SIR,—Once again the problem of the aetiological mechanisms of disseminated sclerosis is under discussion in your columns (*Journal*, June 20, p. 1588). Since my letter (*Journal*, March 30, 1957, p. 760) every patient I have seen with disseminated sclerosis has confirmed the views I then expressed, i.e. that it is a stress disease. I can further state that A.C.T.H. continues to give frequently dramatic results in treatment of relapses of several weeks, or even months, duration. I am still of the opinion that a maintenance dose of this drug should be continued indefinitely in cases whose history is rapidly progressive, but the value of this serious measure is not yet proved, and must await statistical proof by the use of a control series. This is being pursued.—I am, etc.,

J. W. PAULLEY.

Ipswich, Suffolk.

Heart Size in the Dyspnoeic Baby

SIR,—Dr. E. D. Burnard's paper on heart size in the dyspnoeic baby (*Journal*, June 13, p. 1495) is full of interesting points for anyone engaged in midwifery, and his emphasis on clinical phenomena is admirable, but after very careful reading I cannot help thinking that he is describing the heart of two different conditions, one of which is more correctly a sort of continuing apnoea or asphyxia, which would include those with the grunt (unless this was, as it often is, an early sign of hyaline membrane), while the other is dyspnoea due to a pathological condition of the lungs, usually an infection or hyaline membrane. I am not really qualified to speak about premature babies, as I have seen so few of them, but the fact that he mentions the "lapse of time before the development of symptoms after normal birth" compared with the full-term asphyxiated babies, suggests that in these there was a true pathological dyspnoea, while in the others it was probably a continuing asphyxia neonatorum.

The distinction is not merely academic, for as I have many times pointed out—so far without the obstetricians taking any notice—long ago Barcroft showed that respiration is initiated not by oxygen lack but by response to peripheral stimuli, and that "the consequent respiratory response seems to be a fundamental property of the central nervous system." Failure to breathe, therefore, is an indication of depressed cerebral functioning, and until the brain is fully oxygenated the infant's respiratory movements depend much more on the response to peripheral stimuli than to lack of oxygen. Dr. Burnard is therefore quite wrong in stating "Hypoxia is the one element of the asphyxial state which can be directly relieved," for it is even easier and more immediate and effectual to alter the threshold of the cerebral response, by means of a convulsant, so that the brain responds with a full respiratory movement to the stimuli it receives instead of the partial or fitful response of asphyxia. Whether this holds good in the dyspnoeic babies in which the dyspnoea is the perfectly normal response to a pathological condition I do not know, but I should think it would not until the very terminal stages anyhow.

I do not see such cases nowadays, but five weeks ago I was asked by a brother practitioner to help him in a case of foetal distress. I gave the mother a whiff of chloroform while he, with an easy low forceps, extracted what looked like a dead child who had been drowned in a cess pit. There was no detectable heart beat so as rapidly as possible I injected 1 ml. of my pet preparation cardiazol-ephedrine into its left ventricle. Within ten seconds it gave a convulsive movement and then took a slight breath, and after a pause another. I applied some of the old fashioned cutaneous stimulation—which was what according to Barcroft's researches and generations of experience it needed—while the nurse gave it the contents of her Sparklet bulb of oxygen. Within 20 minutes it was breathing well enough to be put into its cot, and not, in agreement with Dr. Burnard, with its head downwards. Thereafter the baby received no special treatment and gave no further cause for anxiety. I think that Dr. Burnard would find small doses of cardiazol-ephedrine much better than the digitalis he mentions, though it must be a small dose, for 0.5 ml. can cause fatal convulsions in a fully oxygenated infant, though 1 ml. is perfectly safe and indeed necessary in a completely asphyxiated one.

It would, I think, have been easier to follow Dr. Burnard's cases if he had given the respiratory rates of his infants, apart from mentioning that they all had rates of over 50 per minute except those with the grunts, and in particular how any improvement in rate—if any—corresponded with diminution of heart size. And finally I would suggest that the slow heart rate that he mentions was probably caused by the same mechanism that causes it in foetal distress during birth, and that it, like the respiratory failure, is in some way connected with the cerebral depression which can be met immediately by stimulation but for which full oxygenation is, of course, the only cure.—I am, etc.,

W. N. LEAK.

Winsford, Cheshire.

Plastic Bags

SIR,—My nephew, aged two-and-a-half, would have been suffocated by a "polythene" bag, which he had pulled over his head (*Journal*, June 6, p. 1463) but for the providential arrival of his mother who found him lying on the floor, blue in the face. The bag had contained potatoes and had come from the greengrocers. it had two air holes in it; in spite of this, because of the soft nature of the material, it had been sucked into mouth and nostrils, completely obstructing them.

I know of the death of a child due to a polythene bag. These bags are lethal.—I am, etc.,

London, S.W.1. PATRICK STACK.

Chemotherapy in Tuberculosis

SIR,—It is acknowledged that at present the best drugs in the treatment of pulmonary and surgical tuberculosis are streptomycin, isoniazid, and P.A.S. (para-aminosalicylic acid), and that initially all three drugs should be given together daily in recognized doses prior to two drugs being given together to complete 18-24 months chemotherapy[1]. The disadvantages of P.A.S. are well-known and it has been suggested that 30-50% of out-patients omit their prescribed P.A.S. in whole or in part[2]. This can be overcome by combined P.A.S. and isoniazid in one cachet.

Intermittent chemotherapy, i.e., bi-weekly streptomycin with daily P.A.S. or daily isoniazid has been tested and condemned. While thrice weekly streptomycin with daily P.A.S. or daily isoniazid is equally frowned upon in certain circles although freely prescribed and recommended by others—your "Any Questions?" expert included[3].

Is there no alternative yet equally satisfactory drug régime to those tested and approved by the Medical Research Council? The alternate day drug regime[4-6] which I first adopted in the Army Chest Centre in 1953 gives excellent results clinically, radiologically, and bacteriologically. To date 92 partial lung resections have been carried out in the Army Chest Centre in 87 Gurkhas (five had bilateral resections) who have been treated on this drug règime. All have done splendidly and post-operative up-grading has been uneventful. All lesions resected at operation are being carefully examined bacteriologically at the Institute of Diseases of the Chest, London (Dr. Lynne Reid and Dr. R. W. Riddell) and at the Army Chest Centre. Results to date would appear to indicate that this drug régime qualifies for the designation "good treatment." This work will be published in due course in *Thorax*. More is still to be known about the best use of the modern anti-tuberculous drugs. Is isoniazid alone as chemoprophylaxis in selected cases good treatment? Where drugs need to be given together, must they always be given every day or might they with advantage, as I suggest, be given together on the same day every second day?—I am, etc.,

Connaught Hospital, Army Chest Centre, Surrey. JOHN MACKAY-DICK.

REFERENCES

1 Ross, J. D., Lancet, 1958, 2, 1125.
2 Lancet, 1957, 2, 881.
3 Brit. Med. J., 1959, 1, 1259.
4 Mackay-Dick, J., and Rothine, N. G., Tubercle, Lond., 1954, 35, 182.
5 ———, Lancet, 1954, 2, 44.
6 ———, and Slattery, D. A. D., Brit. Med. J., 1958, 1, 888.

Obituary

SIR ALAN H. MOORE, Bt., M.B., B.Ch., D.P.H.

Sir Alan Moore, formerly medical officer of health of Rye and of Battle rural district and a well-known authority on the history of sailing ships, died at his home at Battle on June 13, aged 77.

Alan Hilary Moore was born on January 23, 1882, the son of Sir Norman Moore, who was President of the Royal College of Physicians from 1918 to 1922. Educated at Eton, Trinity College, Cambridge, and St. Bartholomew's Hospital, he graduated M.B., B.Ch., in 1911, and took the D.P.H. in 1914. Even when a student and house-physician at Bart's he pursued his study of ships and seamanship, and in the year he qualified he published a paper about diseases at sea in the time of the Tudors and Stewarts. He went to sea as a sub-lieutenant in the R.N.V.R. in 1903, and during the first world war he served as a surgeon-lieutenant. After holding a post as assistant county medical officer in Hampshire, he moved in 1934 to a similar post in East Sussex, where he was also medical officer of health of the Battle rural district and, for a time, of the borough of Rye.

M. I. S. writes: Although I first met him on his retirement, I was able to witness the fruits of Sir Alan Moore's work as medical officer of health to Battle rural district. They were considerable: he laid the foundations for safe water supplies and modern drainage systems. He pioneered the immunization campaign against diphtheria in his rural district and in the Borough of Rye, and it was due to his early efforts that this disease was eliminated before his retirement in 1947.

As a councillor from 1949 to 1958 on the public health committee he was ever active in his desire to ensure the health of the people. He had a deep affection for this lovely Sussex countryside and was outspoken in his efforts to avert any of the ill-effects which might stem from ill-conceived planning. His private life reflected gracious living in an Elizabethan country house with a well-stocked library.

At Eton he obtained his "Boats" as cox in 1898 and remained an active member of the Eton Vikings Club all his life. His knowledge and research into the construction of sailing ships was highly specialized, but he was never pedantic: his great love of the sea and ships was like a breath of fresh air. His research and experience enabled him to write a major work, *The Last Days of Mast and Sail*, in 1925, followed one year later by an essay, *Sailing Ships of War* 1800-1860, which received high praise. In 1926 he was appointed to H.M.S. Victory Technical Committee, serving for 12 years. One of the founders of the Society for Nautical Research, he became a vice-president in 1951. When the *Mayflower* was on her trials in 1957 Sir Alan signed on as an ordinary seaman, performing all the duties, including climbing the rigging. He was a delightful companion, always ready to extend a helping hand. Abhorring any unjust act however trivial, he was the soul of integrity.

He was a grandfather several times, and his family life exemplified the affection in which he was held by all who knew him. A widower, he leaves two sons and two daughters, his heir being Norman Winfrid Moore, senior scientific officer of the Nature Conservancy. We extend our sympathy to the family in their great loss.

HARRY OSBORNE, M.D., D.P.H.

Dr. Harry Osborne, formerly medical officer of health for Salford, died at Sheffield Royal Infirmary on June 21. He was 83 years of age.

Harry Osborne had an outstanding undergraduate career as a medical student at Manchester, gaining many medals and prizes. Qualifying in 1898, he graduated M.B., Ch.B. in the following year and proceeded to the M.D., with commendation, in 1902. After qualification he held several house appointments. Then followed a period in general practice, and after taking the D.P.H. in 1907 he joined the Salford school medical service as an assistant medical officer. Ten years later he became deputy and in 1922 medical officer of health. He retired from these posts in 1941.

In the days when public opinion was far from convinced of the necessity to protect children from diphtheria, Dr. Harry Osborne was responsible for organizing a campaign against a disease which, at times, kept nearly 100 beds occupied at a local hospital. In the field of air pollution he persistently advocated, against opposition as well as apathy, the increasing use of smokeless fuels. Of his hobbies, a consuming interest was philately, particularly the study of the British penny black and twopenny blue stamps. He brought an expert eye and new techniques to the detection and classification of flaws in the plates and printing of stamps, and his beautifully illustrated books are accepted as the foremost contribution on the subject in the philatelic world. The Royal Philatelic Society awarded him the Crawford medal in 1940 for his work on line-engraved penny stamps, and in 1959 he was elected to the roll of distinguished philatelists by the Philatelic Congress of Great Britain.

His wife predeceased him. There were three sons of the marriage—Rowland, who is a plastic surgeon, Derek, who is town clerk of Leyton, Essex, and Norman, who died of poliomyelitis in 1945 while serving with the Forces as a medical officer in Egypt.

ADOLF WINDAUS, Ph.D.

Professor Adolf Windaus, emeritus professor of chemistry at Göttingen University, died at Göttingen on June 9 at the age of 82. In 1928 he was awarded the Nobel Prize for chemistry "for his researches into the sterols and their connexions with the vitamins."

Adolf Windaus was born in Berlin on December 25, 1876. He began the study of medicine at Berlin University, but abandoned this for chemistry, graduating Ph.D. at the University of Freiburg-im-Breisgau in 1899. After a period as lecturer he was appointed to the chair of chemistry at Innsbruck in 1913, moving to the corresponding chair at Göttingen two years later. He retired in 1944.

Windaus's principal contribution to medicine arose from his interest in sterols. Huldschinsky, Hess, and Steenbock had demonstrated the antirachitic effect of ultra-violet irradiation, first on the body itself and then on milk and other foodstuffs. Windaus set out to ascertain what substance in food was converted into the antirachitic vitamin D during irradiation, and he eventually established that it was ergosterol. He later clarified the structure of the vitamin. Windaus also investigated the digitalis and strophanthus glucosides, and produced a number in pure state. Among the honours which came to him were the Adolf Baeyer, Pasteur, and Goethe medals, the honorary degree of M.D. of the University of Göttingen, and the honorary membership of the Chemical Society of London.

E. E. PREST, M.D.

Dr. E. E. Prest, for many years medical superintendent of Glenafton Sanatorium, Ayrshire, died at Dumfries on May 20.

Edward Ernest Prest was born at Sheffield in 1874, the son of the Rev. C. W. Prest, and was educated at Kingswood School, Bath, and at St. John's College, Cambridge, receiving his clinical training at the London Hospital. Graduating M.B., B.Chir. in 1898, he proceeded to the M.D. in 1904. After graduation he held the appointments of house-surgeon at the London Hospital and house-physician at the Brompton Hospital, returning to the London as resident receiving-room officer and assistant anaesthetist. While at the Brompton Hospital he developed a keen interest in the problems of tuberculosis. As a consequence he became physician superintendent of the Glenafton Sanatorium in 1908, remaining there until he retired in 1937.

W. A. M. writes: One of the pioneers in the sanatorium treatment of the disease, Dr. Prest was a very keen physician who made the widest possible use of what facilities were available. Those of us who knew him will remember his widespread use of calcium and his pride in results which even by modern standards were remarkable. He became expert in the use of the early X-ray machines and achieved notable results with a very primitive type of apparatus. He was a classical scholar of considerable note, with a keen and lasting interest in all branches of medicine. During his long stay in Ayrshire he became a very much respected physician and member of the community. He retired to Moffat in 1937, and spent long years quietly among the natural beauties of Dumfries-shire. He was a keen gardener, and until his death at the ripe age of 85 took a lively interest in the affairs of the community of Moffat. He leaves a widow and two sons, to whom our sympathy is extended.

J. T. MACNAB, M.B., B.Chir., D.P.H.

Dr. J. T. Macnab, formerly medical officer of health for Stafford, died on June 4, aged 79.

John Theodore Macnab was born at Dalbeattie, Kirkudbrightshire, on October 27, 1879. From Giggleswick School he entered Christ's College, Cambridge, in 1898, and took first-class honours in part I of the natural sciences tripos and a second-class in part II. In 1901 he was awarded the Broadbank scholarship in natural science. Going on to the London Hospital with a Price entrance scholarship in anatomy and physiology, he qualified in 1905, and graduated M.B., B.Chir., two years later. After qualification he held a number of appointments at the London Hospital, including that of senior resident accoucheur. In 1909 he entered general practice at Balham, returning there after service in the Royal Navy during the first world war. But he had by then developed an abiding interest in preventive medicine, and in 1920 he was appointed senior assistant medical officer under the Salop county council. Having obtained the D.P.H., he left Shrewsbury in 1922 to become medical officer of health for Stafford, holding that appointment until 1936, when he retired and went to live at Eastbourne.

W. D. C. writes: Stafford in the period between the two world wars was a rapidly expanding town, and Macnab had a busy time in dealing with its growing needs. The maternity and child welfare scheme owed much to his devoted work, and he was successful in obtaining the co-operation of the general practitioners of the area. In his school medical work he was equally fortunate in winning the active support of teachers and parents. His clinical work at the isolation hospital was especially congenial to him. He also showed much interest in housing and laid the foundations of many clearance schemes and the rehousing of tenants so displaced. Much of the work of a medical officer of health is unseen, and this especially applies to Macnab's housing work. However, on his retirement the town council gave him a beautifully illuminated address, and his fellow officials left him in no doubt how much they too appreciated him as a man. He retired 23 years ago but is still remembered by many in the town for which he did so much. The town clerk told me recently what a helpful and sympathetic colleague he was.

UNIVERSITIES

UNIVERSITY OF OXFORD

Dr. A. G. M. Weddell has been appointed representative of the University at the seventh International Anatomical Congress to be held in New York in August, 1960.

UNIVERSITY OF CAMBRIDGE

In Congregation on October 18, 1958, the following degrees were conferred:

M.B., B.CHIR.—*J. D. J. Parker.
M.B.—*R. D. Cohen, *H. P. R. Bury, *I. R. Carr, J. S. Elkington, R. K. Jackson, R. J. Read, A. J. Taylor
*By proxy.

In Congregation on February 7 the following degrees were conferred:

M.D.—*P. H. A. Seath, J. P. Reidy, J. D. S. Knight.
M.B., B.CHIR.—*D. P. S. Heath, *M. I. Lander.
M.B., J. R. Bartlett, R. B. Woodd-Walker, R. P. Wilding, J. D. M. Stewart, D. J. Richards.
*By proxy.

Dr. D. G. Chalmers has been appointed University Haematologist to Addenbrooke's Hospital in the Department of Pathology with tenure from July 1, 1959, for three years.

Drs. P. A. G. Monro and C. C. D. Shute have been reappointed University Lecturers in the Department of Anatomy with tenure from October 1, 1959, to the retiring age.

Dr. J. T. Fitzsimons has been appointed a University Demonstrator in the Department of Physiology with tenure from October 1, 1959, for three years.

Dr. D. H. M. Woollam has been elected into an Official Fellowship of Emmanuel College with effect from August 1, 1959, associated with his office of University Lecturer in Anatomy.

In Congregation on February 21 the degree of M.A. was conferred on Dr. J. H. Cullen, senior assistant in research in medical psychology, and the degree of M.B. on W. E. I. Forsythe-Jauch.

UNIVERSITY OF LONDON

The following degrees were awarded in January:
M.D.—A. S. V. Burgen, J. A. Dossett, D. L. Walker, J. L. Turk.
M.S.—J. Whitwell.

Dr. H. W. Bunjé has been elected and Dr. N. A. Thorne re-elected to membership of the Standing Committee of Convocation for a period of three years from January, 1959.

UNIVERSITY OF BIRMINGHAM

Sir Arthur Thomson, Mr. A. L. d'Abreu, Professor W. Melville Arnott, and Dr. A. G. W. Whitfield have been appointed representatives of the University on the Standing Joint Committee of the University, the United Birmingham Hospitals, and the Birmingham Regional Hospital Board for the year April 1, 1959, to March 31, 1960.

Professor A. B. MacGregor has been appointed a representative of the University on the Central Counties Dental Postgraduate Committee for the triennial period 1959–62.

Professor J. R. Squire has been appointed Deputy Dean of the Faculty of Medicine for the period October 1, 1959, to September 30, 1961.

The title of University Research Fellow in the Department of Paediatrics and Child Health has been given to Dr. P. M. Jeavons, consultant psychiatrist to All Saints' Hospital, Birmingham, for two years in the first instance from April 1, 1958, and in the Department of Experimental Pathology to Dr. M. E. Abrams, Endowment Fund Research Assistant, United Birmingham Hospitals, during the tenure of his present appointment.

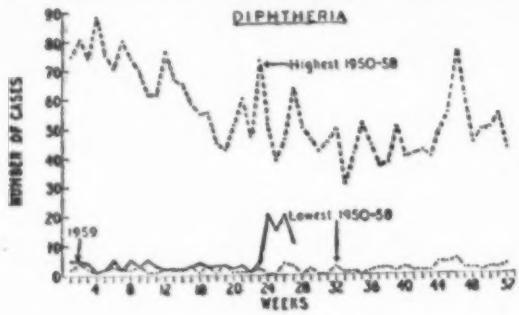
The title of University Clinical Lecturer in the subject indicated in parentheses has been given to the following members of the staff of the United Birmingham Hospitals: Mr. P. Dawson-Edwards (Surgery), Dr. E. T. Mathews (Anaesthetics), Dr. E. A. Fairburn (Dermatology), and Dr. G. A. Newsholme (Radiotherapy).

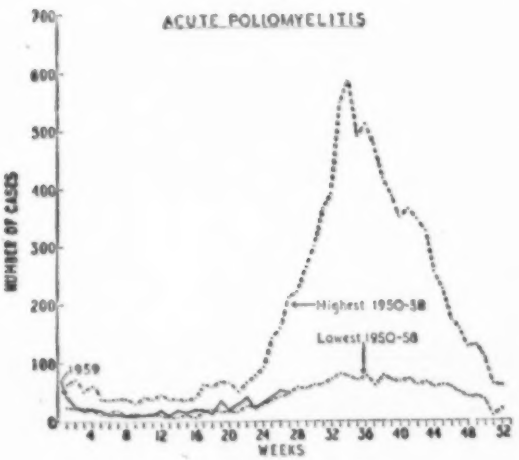
TODAY'S PROSCRIPTION

The above photograph of pickets outside B.M.A. House was taken on July 15.

(1) "British Medical Journal Printed by Blacklegs".
(2) "Doctors! Remove Scabs, Boycott British Medical Journal".
(3) "Doctors! Proscribe British Medical Journal Now Black".
(4) "British Medical Association! Break Assoc. with Black Printers".

Vital Statistics





Any Questions?

Vitamin B_{12} in Diabetic Neuritis

Q.—*It is known that 100 g. of vitamin B_{12} every three weeks is sufficient to maintain the blood at a normal level in pernicious anaemia. Why is it that 1,000 g. vitamin B_{12} daily is advised in diabetic neuritis?*[1] *Could overdosage of B_{12} cause damage to the bone marrow by over-stimulation?*

A.—There is no evidence of vitamin B_{12} deficiency in diabetic neuropathy and the use of B_{12} injections for the relief of pain in this condition is empirical, as it also is in trigeminal neuralgia. It is difficult to assess the value of the treatment, but in some cases it does seem to be helpful in reducing pain; it might well be that smaller doses than those suggested in the article[1] would be equally effective. There does not appear to be any danger of damaging the bone marrow when the larger doses are given.

REFERENCE

[1] *Brit. med. J.*, 1958, 2, 1483.

Stability of Trichlorethylene

Q.—*Does trichlorethylene keep well over a number of years?*

A.—Trichlorethylene is stable for long periods provided that it is stored in a cool place, in the closed, light-proof containers in which it is supplied. It is, however, readily decomposed by strong light or by contact with hot surfaces. For example, when left in an ordinary clear glass bottle for three weeks it was found to have undergone considerable decomposition, with the formation of phosgene and hydrochloric acid. In an anaesthetic apparatus it should be placed in a tinted bottle. It should be changed every few days, and should never be used if it has been exposed for a long or unknown period to the action of light.

Vitamin Creams

Q.—*Have vitamin creams any therapeutic value?*

A.—Not a great deal is known of the effects of topical application of vitamins in humans, and experiments in animals have been variously interpreted. Vitamins are necessary for epidermal metabolism and they can be absorbed through the skin. The clinical use of creams containing vitamin A, especially in an unsaturated fatty acid base, which is itself beneficial, often gives clinical improvement in some keratolytic dermatoses while it is being used. In animals they produce some epidermal hypertrophy and influence hair growth.

REFERENCE

[1] Lawrence, D. J., and Bern, H. A., *J. invest. Derm.*, 1958, 31, 313.

Vitamins for Fevers

Q.—*Is there any justification for prescribing vitamin B complex in common acute febrile conditions, or should one wait for clinical signs of deficiency?*

A.—Vitamin supplements are indicated in those in whom a borderline state of nutrition is suspected because of a history of dietary inadequacy, alcoholism, anorexia nervosa, gastrointestinal disease, poverty, old age, etc. But these conditions are infrequently associated with the common run of febrile conditions to which the question refers. There is no firm scientific evidence, based on large, carefully controlled clinical trials, to justify prescribing B complex routinely in the common acute febrile conditions seen in general practice.

The important problem of nutrition in infections was the subject of a conference held in 1955 by the New York Academy of Sciences. The proceedings[1] make interesting reading, with a balanced admixture of scientific data and speculation, as indeed a successful symposium should be. One participant, Dr. M. Suzman, of Johannesburg, questioned the validity of the results of animal experiments which indicate that certain induced dietary deficiencies increase or decrease susceptibility to infections, certainly in so far as these results are applied to man. In his experience even the poorly nourished patient, deficient in vitamins, can combat infections, once established, as well as the adequately nourished subject.

Although the question does not directly refer to the use of antibiotic-vitamin combinations, this aspect of it is a natural corollary. Once again there are no adequate controlled trials to support the routine use of vitamins with antibiotics in the common acute febrile conditions seen in general practice. Some studies have demonstrated that antibiotic administration has exerted a sparing action on the requirement of B vitamins, and other studies have suggested that antibiotics contribute to a deficiency of this group. Furthermore, it is just possible that antibiotics may induce vitamin deficiency by competitive blockage of intracellular metabolism. If this were so, administration of vitamins might even lessen the effectiveness of antibiotics.[2]

REFERENCES

[1] *Ann. N.Y. Acad. Sci.*, 1955, 63, 147.
[2] Goldsmith, G. A., *Antibiot. Ann.*, 1955-1956, p. 266. New York.

COMING EVENTS

European Society of Haematology.—7th Congress to be held in London, September 7–12. Further information from the Secretary, Dr. E. NEUMARK, Department of Pathology, St. Mary's Hospital, London, W.2.